Control of a Model of DNA Division via Parametric Resonance

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- Study internal resonance, energy transfer, activation mechanism, and control of a model of DNA division via Parametric Resonance.
  - To provide a method to control real DNA division by EM fields.
  - To understand how enzymes initiate DNA open state dynamics.

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- Background and Motivation
  - A Model of DNA Division.
  - An Intriguing Phenomenon of Structured Activations that the model exhibits in previous Numerical Studies.
- Our Results on studying this phenomenon **Analytically**:
  - Use data to show it is appropriate to use Reduced Models.
  - 0:1 Resonance, Partial Averaging to obtain Average Equations.
  - Use Average Equations to reveal Activation Mechanism, and to estimate analytically Minimum Activation Energies.
  - Analytical results match numerical simulations of Full Model.

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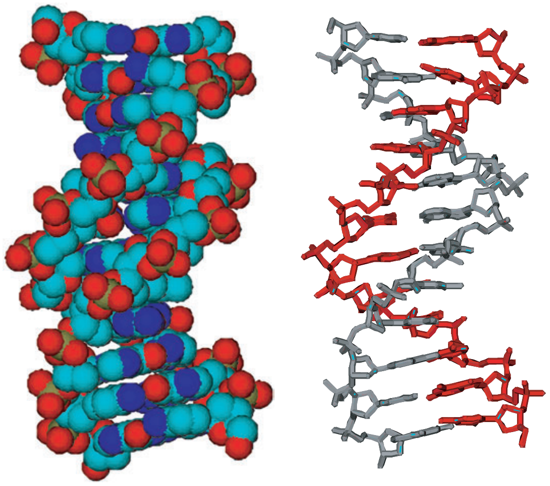
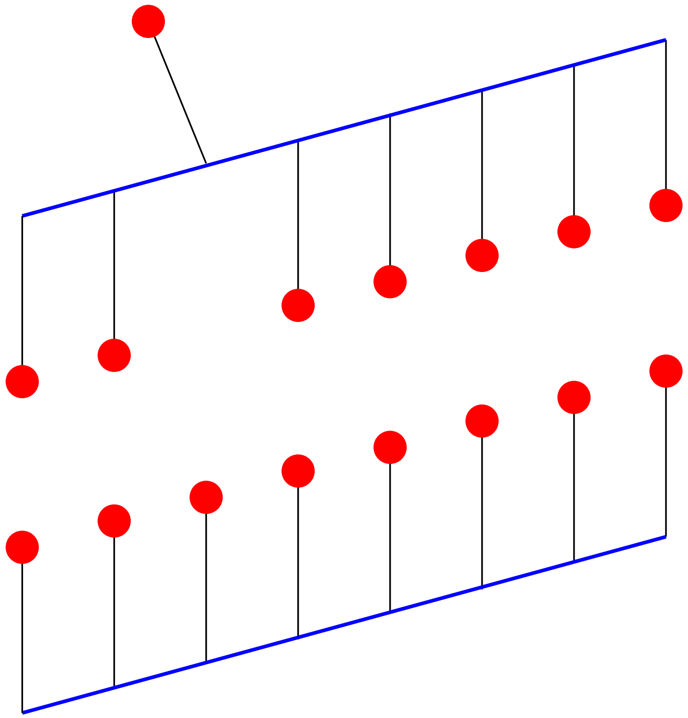
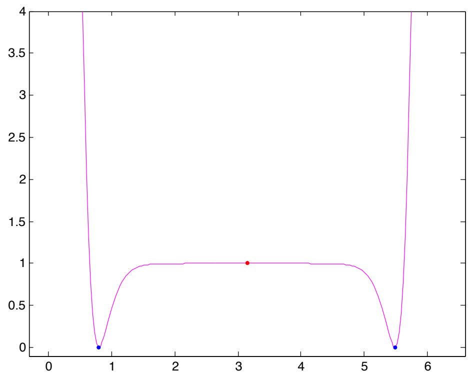
  - Use Average Equations to reveal Activation Mechanism, and to estimate analytically Minimum Activation Energies. Analytical results match numerical simulations of Full Model.
- Building on our understanding of its Internal Dynamics, able to control division of this DNA model via Parametric Excitation, that is in resonance with its Internal Trigger Modes.

A Model of DNA Division (I)

- A chain of pendula that rotate about axis of a fixed backbone, with angle θ_k measured from upward position.
  - The pendula interact with nearest neighbors along the backbone through harmonic torsional coupling, and
  - with pendula on the opposing immobilized strand through a Morse potential.







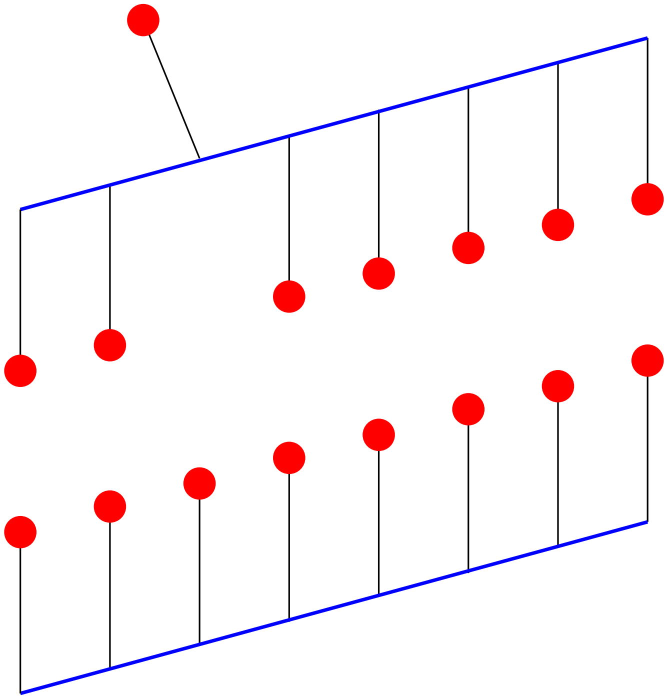
A Model of DNA Division (II)

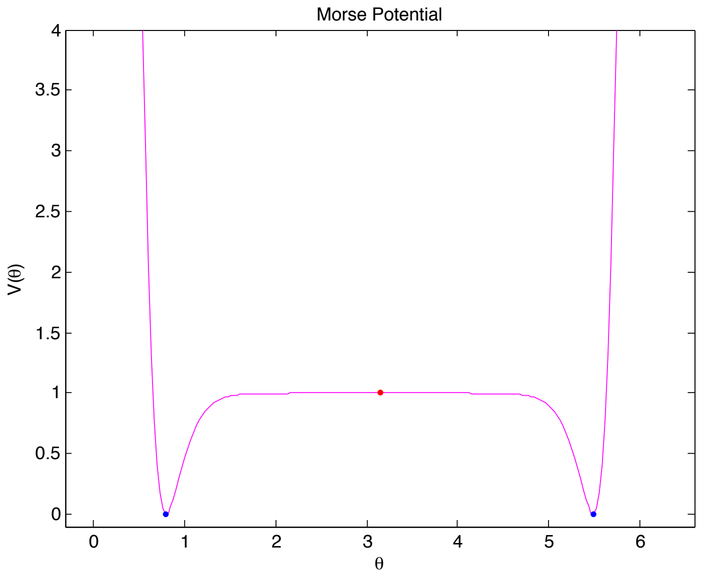
- Non-dimensional Hamiltonian for these n coupled pendula

$$H(\theta, p_\theta) = \sum_{k=1}^{n} \left[\frac{1}{2} p_{\theta k}^2 + \frac{1}{2}(\theta_k - \theta_{k-1})^2 + \epsilon \left(e^{-a(1+\cos\theta_k - d_0)} - 1 \right)^2 \right]$$

  with periodic boundary condition $\theta_n = \theta_1$.

- Decaying coefficient $a = 7$; Equilibrium distance $d_0 = 0.3$; Amplitude $\epsilon = 1/1400$. Parameter values are chosen to best represent typical values for DNA division.





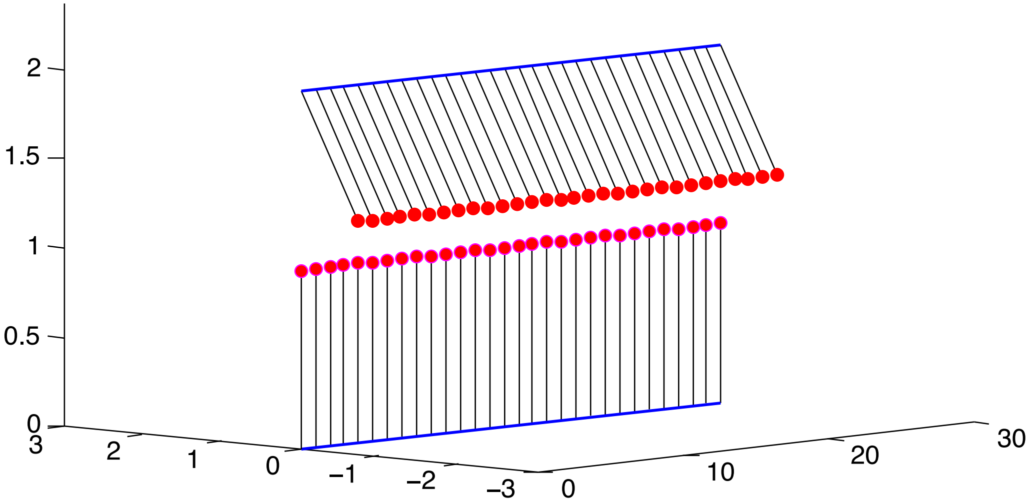
A Model of DNA Division (III)

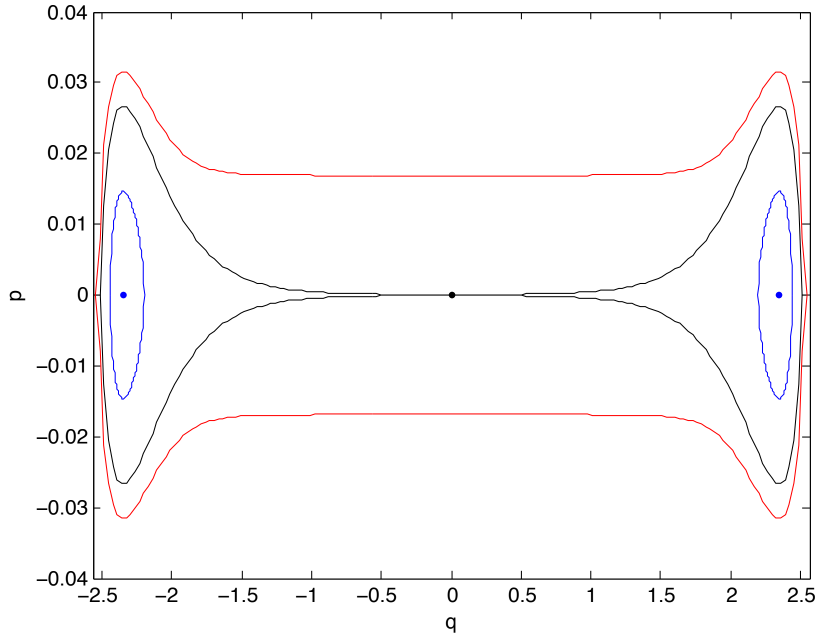
- For analytical study, Hamiltonian of 30 coupled pendula is used

$$H(\theta, p_\theta) = \sum_{k=1}^{30} \left[\frac{1}{2} p_{\theta k}^2 + \frac{1}{2}(\theta_k - \theta_{k-1})^2 + \epsilon \left(e^{-a(1+\cos\theta_k - d_0)} - 1 \right)^2 \right]$$

  - This is the same number of pendula used in numerical studies by Eisenhower and Mezic at UCSB.
  - It has captured all interesting phenomena of larger systems.

- Model of 30 coupled pendula.



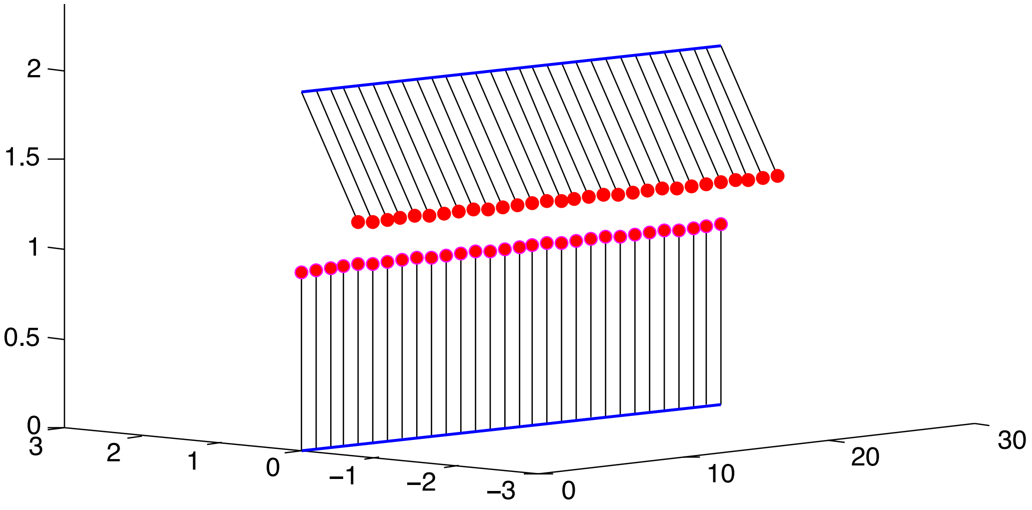


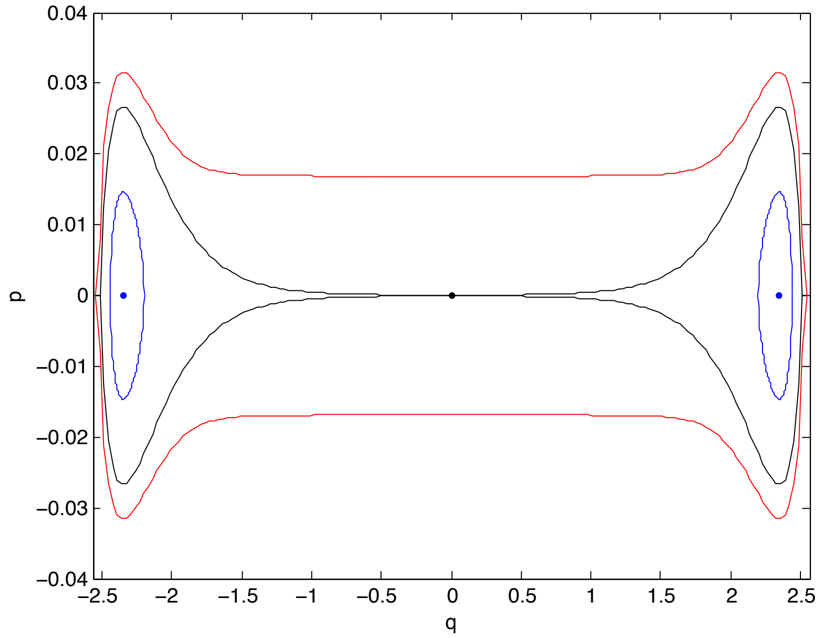
A Model of DNA Division (IV)

- The Hamiltonian of 30 coupled pendula

$$H(\theta, p_\theta) = \sum_{k=1}^{30} \left[\frac{1}{2} p_{\theta k}^2 + \frac{1}{2}(\theta_k - \theta_{k-1})^2 + \epsilon \left(e^{-a(1+\cos\theta_k - d_0)} - 1 \right)^2 \right]$$

- Before studying model, instructive to look at 1 pendulum (n=1).
- Phase space of a pendulum in Morse potential without coupling.
  - 2 stable equilibria at $(\pm\theta_e, 0)$, 1 saddle at $(0, 0)$.
  - **Separatrix**, oscillation near equilibria, flipping across saddle.
- Model of 30 coupled pendula:



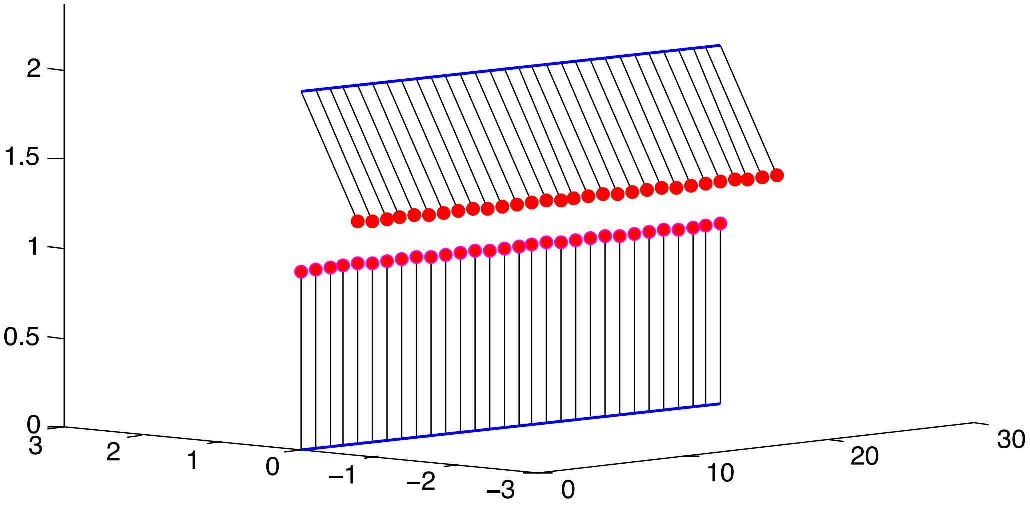


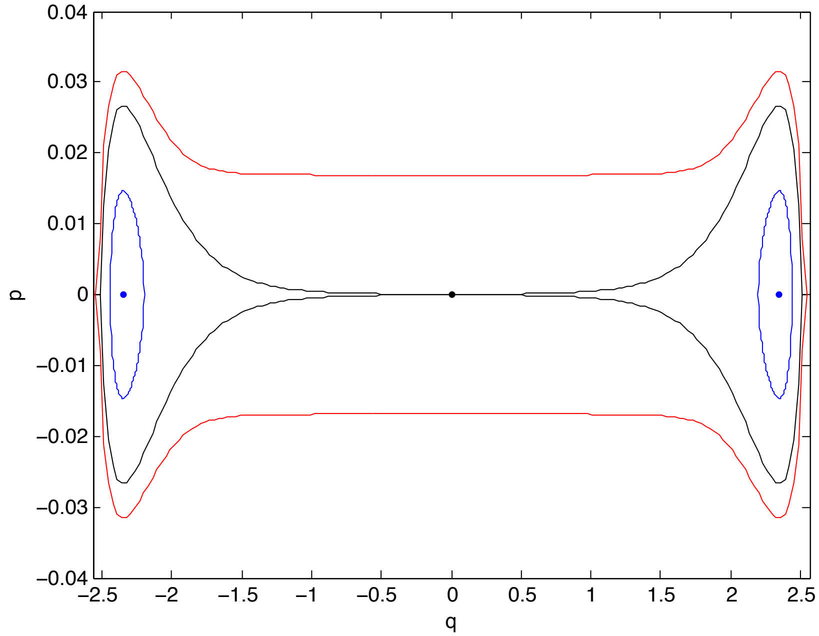
A Model of DNA Division (V)

- **30-coupled** pendula has similar but much complicated behaviors.

$$H(\theta, p_\theta) = \sum_{k=1}^{30}\left[\frac{1}{2}p_{\theta k}^2 + \frac{1}{2}(\theta_k - \theta_{k-1})^2 + \epsilon\left(e^{-a(1+\cos\theta_k - d_0)} - 1\right)^2\right]$$

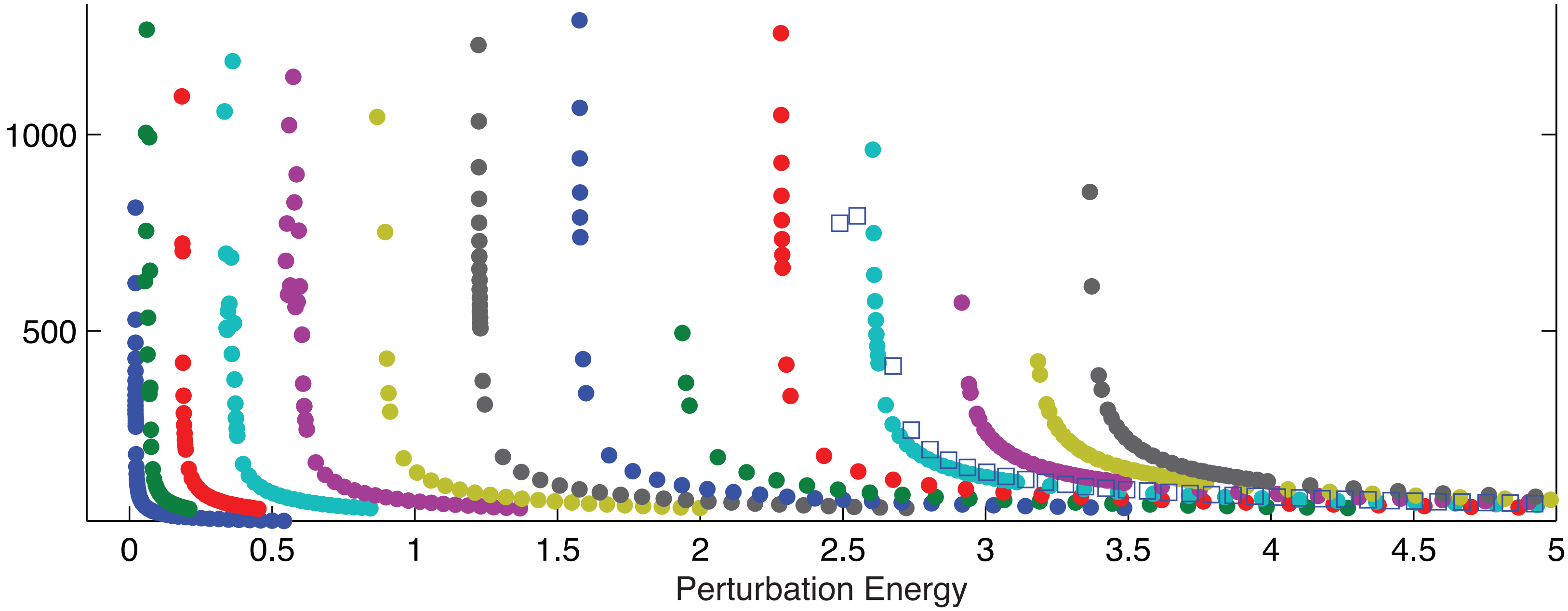
- 2 stable equilibria when $\theta_k = \pm\theta_e$, 1 rank one saddle when $\theta_k = 0$.
  - For small energy, liberate near stable equilibria (global minima).
  - For large enough energy, move collectively from one energy basin to the other and flip across a rank 1 saddle.
- Model of 30 coupled pendula:





Phenomenon of Structured Activations (I)

- Previous studies, mainly numerical, showed that this model exhibits an intriguing phenomenon of structured activations:
  - While the system is **robust to noise**, it is sensitive to certain specific fine scale modes that can trigger the division.
  - See Mezic [2006], Eisenhower and Mezic [2007, 2010], Eisenhower [2009], Du Toit, Mezic, and Marsden [2009].
- Figure (Eisenhower [2009]): Show initial amount of energy injected for various types and shapes of actuation vs time to DNA division.



Phenomenon of Structured Activations (II)

- To appreciate figure and claim shown above, need to introduce Fourier modal coord. q related to system coord. ($\theta = Mq$):

$$\theta_k = \sqrt{\frac{2}{n}} \sum_{\alpha=0}^{\frac{n}{2}-1} \left[\frac{q_0}{\sqrt{2}} + cos\,\frac{2\pi k\alpha}{n} q_\alpha + \frac{(-1)^j q_{\frac{n}{2}}}{\sqrt{2}} + sin\,\frac{2\pi k\alpha}{n} q_{\frac{n}{2}+\alpha} \right].$$

- FMC reveal **natural dynamics** of the system by diagonalising linear coupling terms and rewriting the Hamiltonian as follows

$$H(q,p) = \sum_{\alpha=0}^{n-1} \left(\tfrac{1}{2} p_\alpha^2 + \tfrac{1}{2} \omega_\alpha^2 q_\alpha^2 \right) + \epsilon \sum_{k=1}^{n} U\Big(\sum_{\beta=0}^{n-1} M_{k\beta} q_\beta\Big)$$

where $U(\theta) = (e^{-a(1+\cos\theta-d_0)} - 1)^2$ is Morse potential function.

- **Now**, the model can be seen as a small perturbation of n oscillators with frequencies ω_α : $\omega_\alpha^2 = 2 - 2\,cos\,(2\pi\alpha/n)$, $\alpha = 0, ..., n-1$.

Phenomenon of Structured Activations (III)

- This can also be seen clearly if we write EOM in Lagrangian form

$$\begin{aligned}\ddot{q}_0 &= \epsilon F_0(q_0, q_1, ..., q_{n-1}) \\ \ddot{q}_\alpha + \omega_\alpha^2 q_\alpha &= \epsilon F_\alpha(q_0, q_1, ..., q_{n-1})\end{aligned}$$

  with modal frequencies $\omega_\alpha^2 = 2 - 2\,cos\,(2\pi\alpha/n), \alpha = 1, ..., n-1.$

- The coordinate of 0th (Fourier) mode, q_0, given as follows

$$q_0 = \frac{1}{\sqrt{n}} \sum_{k=1}^{n} \theta_k = \sqrt{n}\bar{\theta}$$

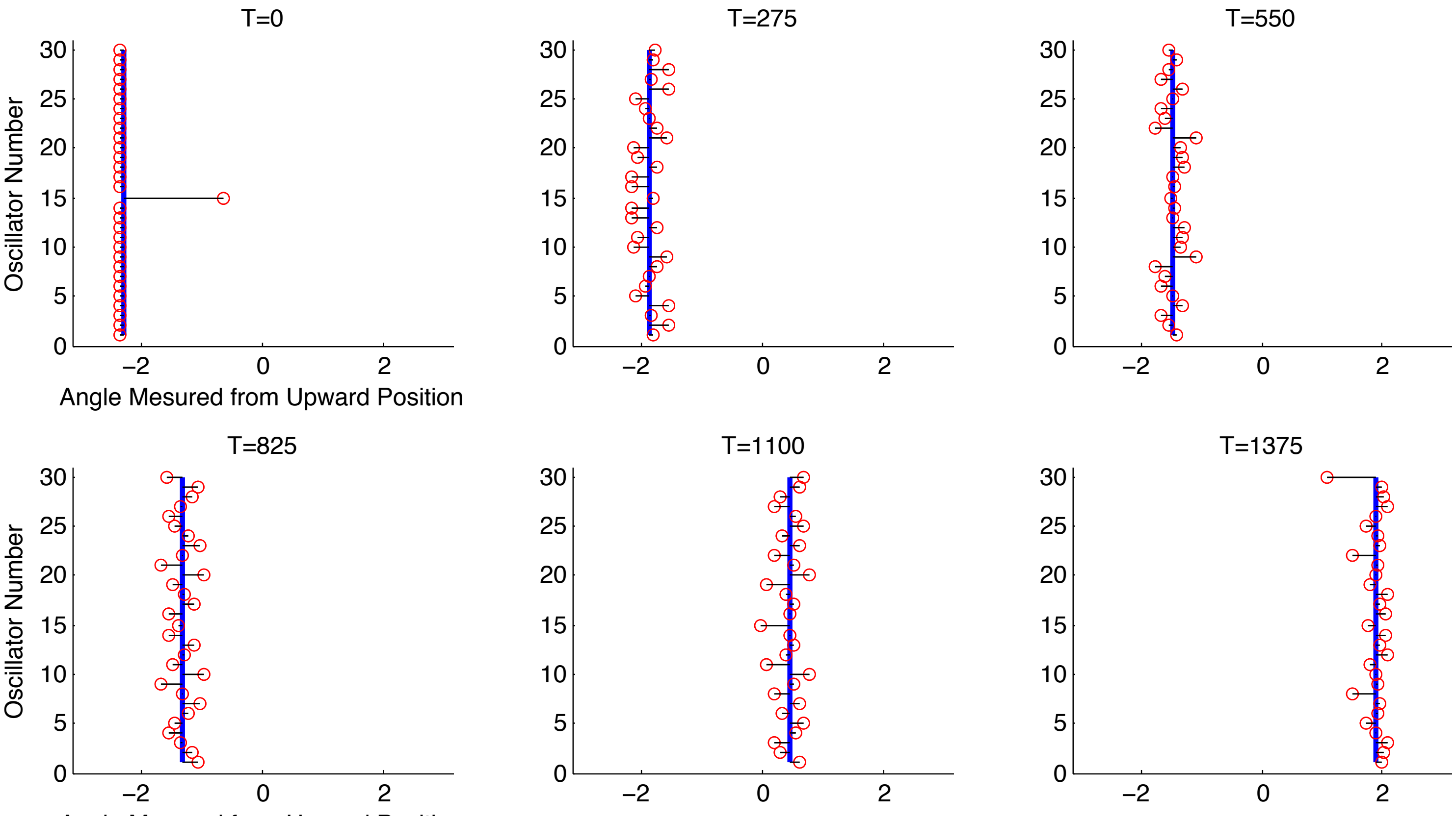
  is the average angle $\bar{\theta}$ of pendula (except a factor of $\sqrt{n}$).

- It plays the special and important role as the collective variable, reaction coordinate, and slow variable, as will be shown later.

- Other $(n-1)$ modal coordinates q_α are the bath coordinates, and the fast variables.

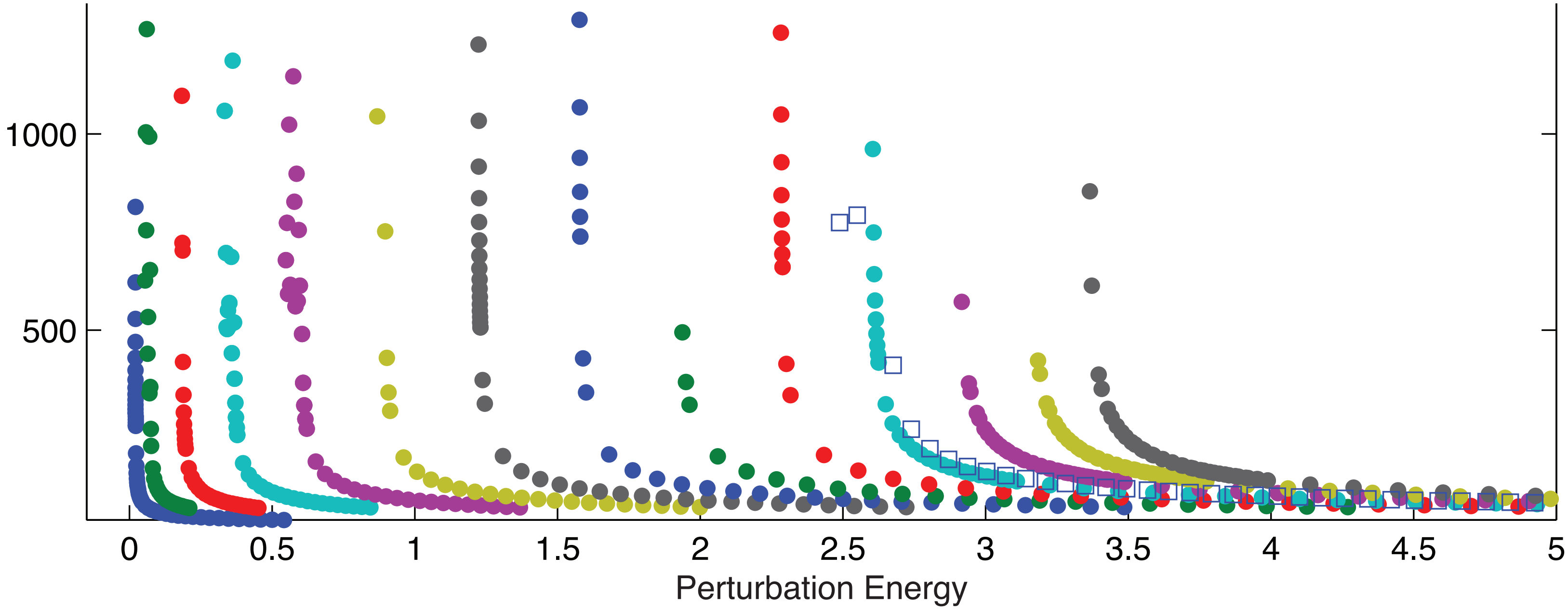
Phenomenon of Structured Activations (IV)

- The role of $q_0 = \sqrt{n}\bar{\theta}$ can be seen from sequence of 6 snapshots of evolution of 30 pendula from **equilibria** $-\theta_e$ to θ_e across $\theta = 0$.
- For simplicity, only one pendulum is perturbed as initial activation.
- Because **coupling** is much stronger than **nonlinearity**, transition is collective, closely follow average (**thick** blue line).
- Average angle q_0 can be used to determine time to division.



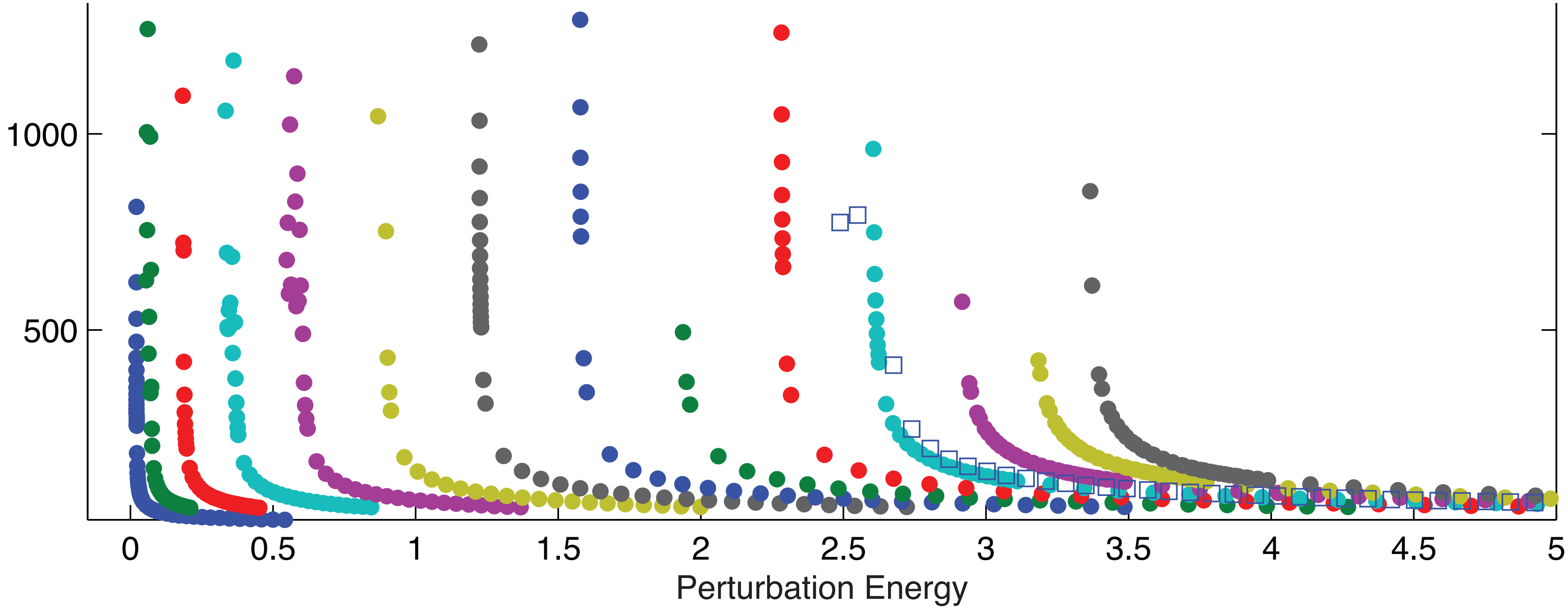
Phenomenon of Structured Activations (V)

- **Now**, initial activation is chosen as a single Fourier mode, $p_\gamma(0)$, and its amplitude modified to vary the amount of activation energy.
- Time to division determined when average angle q_0 cross $q_0 = 0$.
- A curve is obtained that shows the amount of activation energy vs the time to DNA division for each Fourier mode (first 14 modes).
- Each has asymptote at low energy limit (min. activation energy).
- White "☐"s show the data for **random noise**.



Phenomenon of Structured Activations (VI)

- The minimum activation energy (MAE) depends significantly on the way this energy is injected into the system.
- While the system is **robust to noise**, it is sensitive to certain specific fine scale modes that can trigger the division.
- Want to develop analytical method to reveal activation mechanism and to compute MAEs.
- Want to develop methods for controlling DNA division via EM fields and reveal how enzymes initiate DNA open states dynamics.



Nearly $0:1$ Resonance and Partial Averaging

- **Analytical study**: recall EOM are given by

$$\begin{aligned} \ddot{q}_0 &= \epsilon F_0(q_0, q_1, ..., q_{n-1}) \\ \ddot{q}_\alpha + \omega_\alpha^2 q_\alpha &= \epsilon F_\alpha(q_0, q_1, ..., q_{n-1}) \end{aligned}$$

with modal frequencies $\omega_\alpha^2 = 2 - 2\,cos\,(2\pi\alpha/n), \alpha = 1, ..., n-1$. (Note: ω_α varies from 0.2091 to 2.)

- The reactive mode (0th mode) forms a nearly $0:1$ **resonance** with any other mode, each of which has an $O(1)$ frequency

$$m\omega_0 + 0\omega_\alpha \approx 0, \qquad \text{with } m = 1.$$

- This fact leads to **small denominators** and **coupling terms** in the corresponding **averaged equations** or **normal form**.

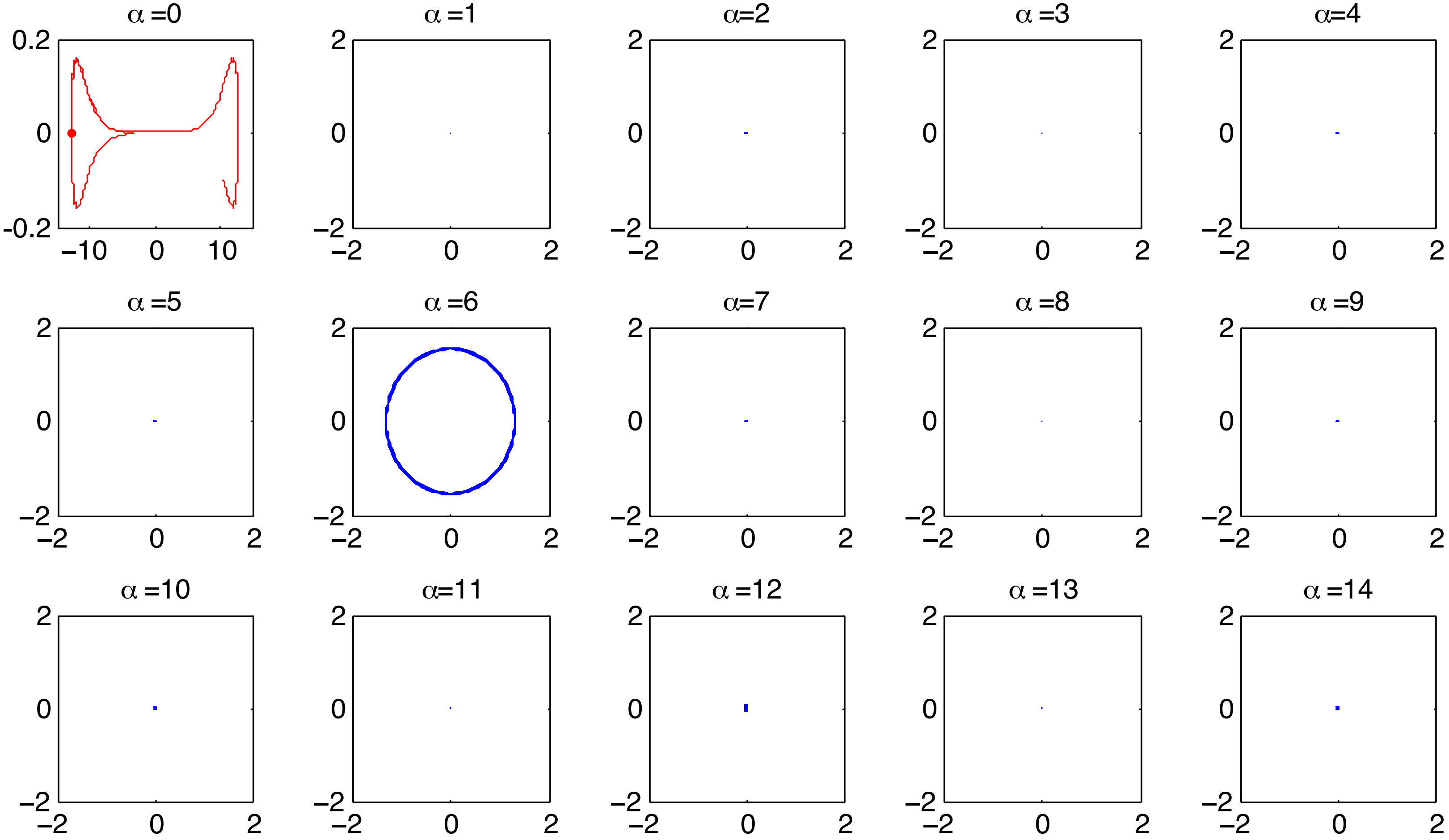
Nearly $0:1$ Resonance and Partial Averaging

- Other modal frequencies, are not rationally commensurate and do not have significant time scale separation.
  We don't expect strong resonance among them.
- Expect nearly $0:1$ **resonance** will be main focus of our study.
- While Eisenhower and Mezic had not mentioned $0:1$ resonance, they did apply Arnold's method of partial averaging to a truncated Hamiltonian in the study of a chain of Duffing oscillators.
- In their [2010] paper, the reason they gave for studying the Duffing case was that "The exponential form of the Morse potential makes analytical progress difficult,..."
- However, since we had not seen this kind of simplification in the DNA literatures before, we decided to keep the Morse potential and were able to obtain a number of interesting results.

Two Mode Truncation Is Adequate (I)

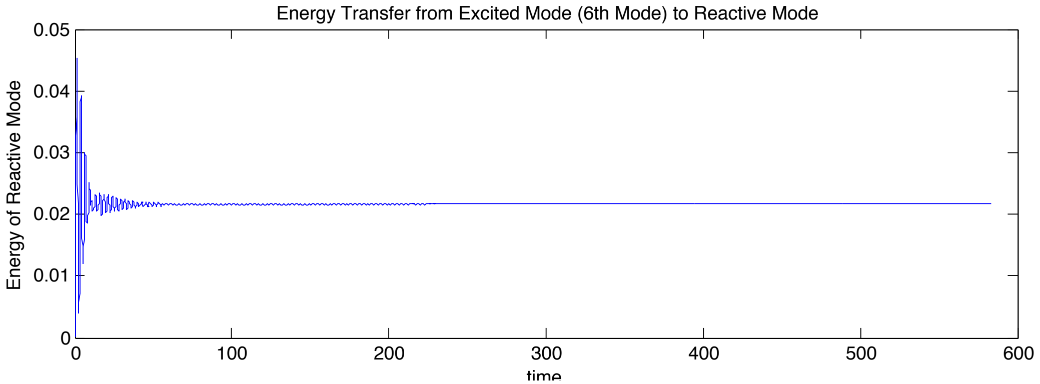
▶ Projections of a sample trajectory on phase spaces of first 15 modes. Initial activation chosen to be single 6th mode $(q_0^e, \ldots, p_6(0), \ldots)$.

- energy transfer over-whelmingly from excited to reactive mode,
- only an extremely small amount of energy transfers from the excited mode to 1 or 2 other modes via near resonances.

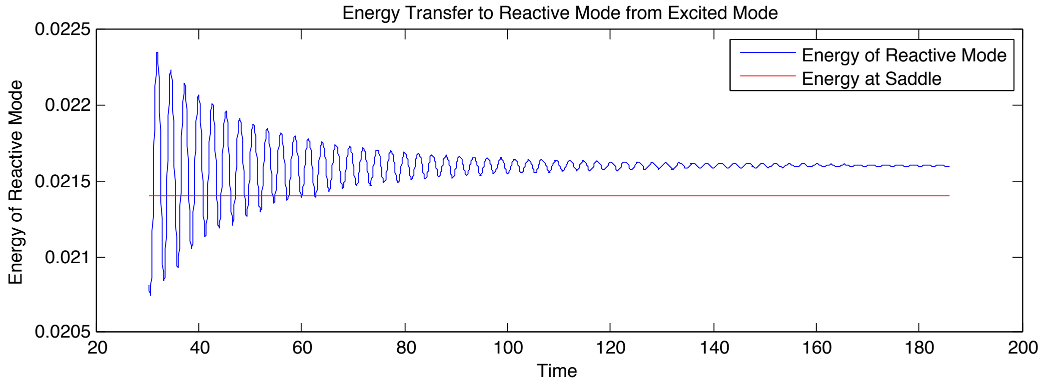


Two Mode Truncation Is Adequate (II)

- Show **time history** of energy in reactive mode.
- Resonance transfers energy from excited mode into reactive mode and cause reactive energy to increase and surpass energy at saddle.
- Expect **2-modes/3-modes truncations**, (truncated system of reactive mode, excited mode, & perhaps a mildly affected mode), should provide an adequate **reduced model** for analytical studies on $0:1$ resonance, energy transfer, and activation mechanisms.



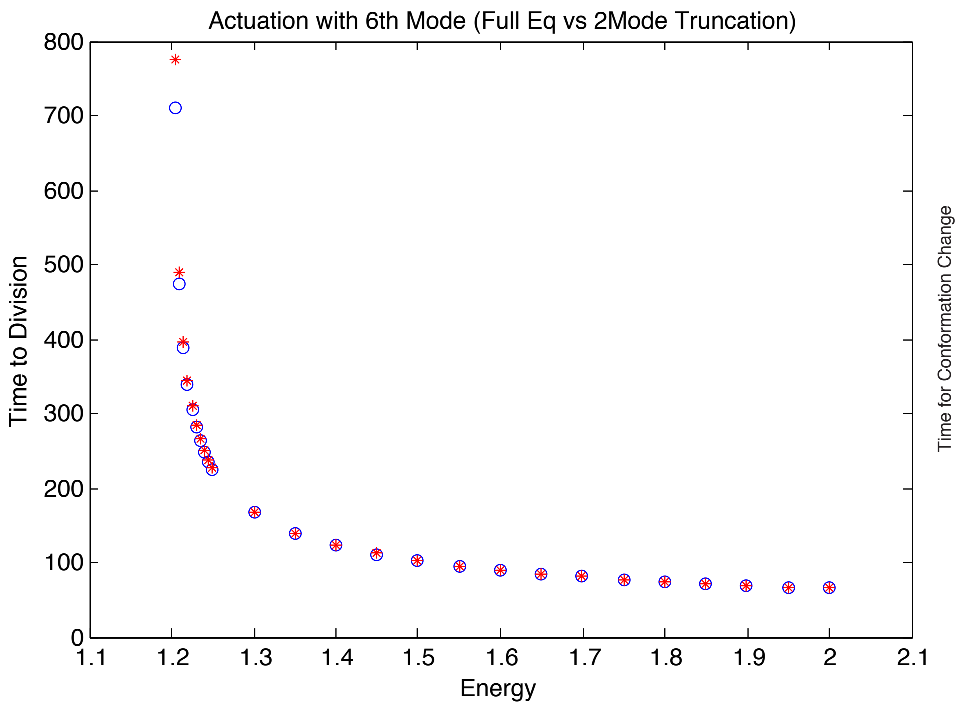
Energy Transfer from Excited Mode (6th Mode) to Reactive Mode

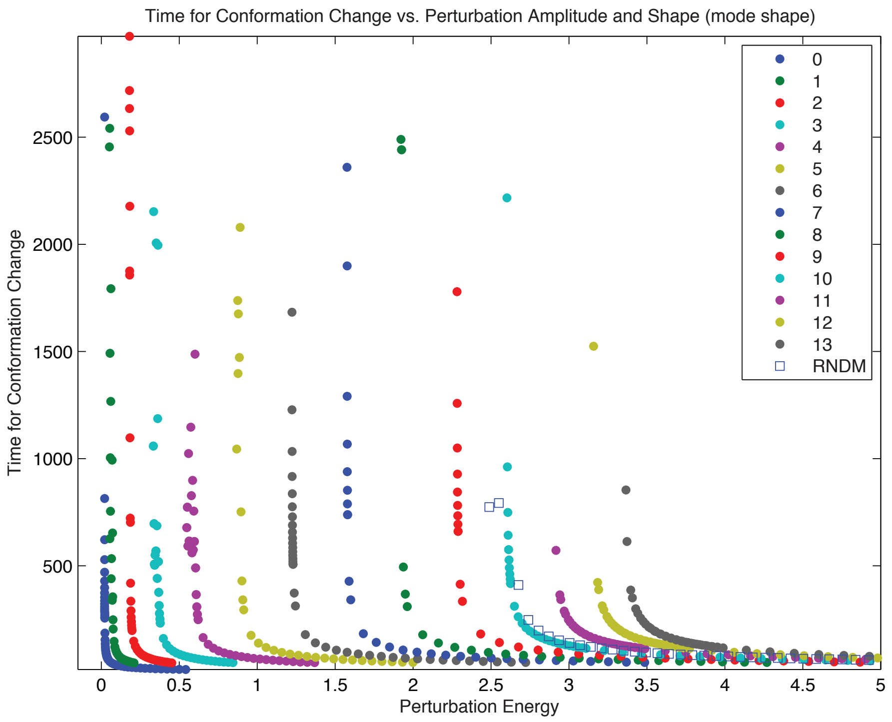


Energy Transfer to Reactive Mode from Excited Mode

Two Mode Truncation is Adequate (III)

- Show **Activation Energy** vs **Time to DNA Division**
  - blue ”o”s are data points for full equations (30 modes);
  - red ”*”s are data points for 2 mode truncation (0th & 6th mode).
- Both have almost the same **minimum activation energy** 1.205.
- Their **time to division** differs very little if **activation energy** is slightly larger than MAE.
- All data from simulation confirm: 2 mode truncation is adequate.





Nearly $0:1$ Resonance and Partial Averaging

- Ready to apply **partial averaging**
  - to obtain average equations for reduced models, and use them
  - to study activation mechanism & compute MAE for each mode.
- For 2 mode truncation (0th and γth mode), Lagrangian EOM is

$$\begin{aligned} \ddot{q}_0 &= \epsilon F_0(q_0, q_\gamma) \\ \ddot{q}_\gamma + \omega_\gamma^2 q_\gamma &= \epsilon F_\gamma(q_0, q_\gamma). \end{aligned}$$

Notice: q_0 is the slow variable and q_γ is the fast variable.

- Its correspondent Hamiltonian is

$$H_2^\gamma(q,p) = \sum_{\alpha=\{0,\gamma\}} \left(\tfrac{1}{2}p_\alpha^2 + \tfrac{1}{2}\omega_\alpha^2 q_\alpha^2\right) + \epsilon \sum_{k=1}^{n} U\Big(\sum_{\beta=\{0,\gamma\}} P_{k\beta} q_\beta\Big)$$

- Since partial averaging of **Lagrangian equations** is equivalent to partial averaging of its **Hamiltonian**,
and our main concern is on energy transfer,
we preferred to use Hamiltonian formulation in this study.

■ Partial Averaging and Average Reduced Hamiltonian

- First, **expand** Morse potential U, which involves exponential function, as a polynomial of 26 degrees at $\theta = 0$.

$$H_2^\gamma(q,p) = \sum_{\alpha=\{0,\gamma\}} \left(\tfrac{1}{2}p_\alpha^2 + \tfrac{1}{2}\omega_\alpha^2 q_\alpha^2\right) + \epsilon \sum_{k=1}^{n}\sum_{j=0}^{26} a_j\Big(\sum_{\beta=\{0,\gamma\}} P_{k\beta}q_\beta\Big)^j$$

- Then, **use** action angle coordinates

$$q_\gamma = \sqrt{2I_\gamma/\omega_\gamma}\sin\phi_\gamma, \qquad p_\gamma = \sqrt{2I_\gamma\omega_\gamma}\cos\phi_\gamma.$$

and **rewrite** reduced Hamiltonian as $H_2^\gamma(q_0, p_0, I_\gamma, \phi_\gamma)$.

- Notice: Besides q_0, p_0, action I_γ is also a slow variable.
- The **average reduced Hamiltonian** can be obtained by **averaging** the only fast variable ϕ_γ

$$\bar{H}_2^\gamma(\bar{q}_0, \bar{p}_0, \bar{I}_\gamma) = \tfrac{1}{2\pi}\int_0^{2\pi} H_2^\gamma(q_0, p_0, I_\gamma, \phi_\gamma)d\phi_\gamma$$

Average Reduced Hamiltonian

- After renaming variables, **average reduced Hamiltonian** is

$$\bar{H}_2 = \frac{1}{2}y^2 + \omega I + \epsilon\left(na_0 + \sum_{k=0}^{13} c_{2k}(I)x^{2k}\right)$$

  - $x = \bar{q}_0, y = \bar{p}_0$ are Cartesian coordinates of 0th mode;
  - $I = \bar{I}, \omega = \omega_\gamma$ are action and frequency of the other mode;
  - $c_{2k}(I)$, polynomials in I; $\epsilon na_0 = 0.0214$: energy value at saddle.

- **Average reduced Hamiltonian equations** are

$$\dot{x} = y, \qquad \dot{I} = 0$$

$$\dot{y} = -\epsilon\left(\sum_{k=1}^{13} 2kc_{2k}(I)x^{2k-2}\right)x; \qquad \dot{\phi} = \omega + \epsilon\left(\sum_{k=0}^{13} \frac{dc_{2k}}{dI}x^{2k}\right)$$

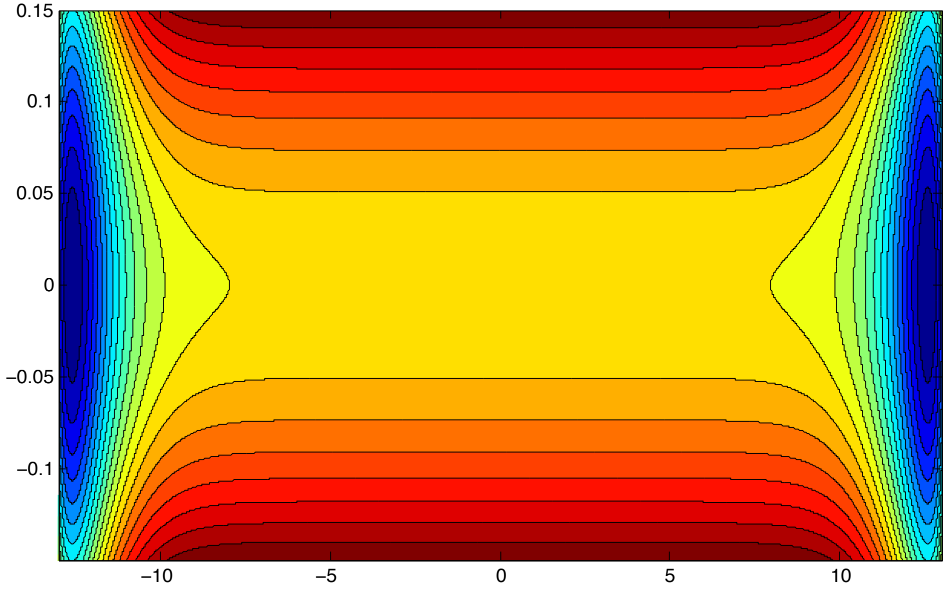
I is a constant of motion. Averaged equations and averaged phase space structures of the reactive mode are parametrized by I.

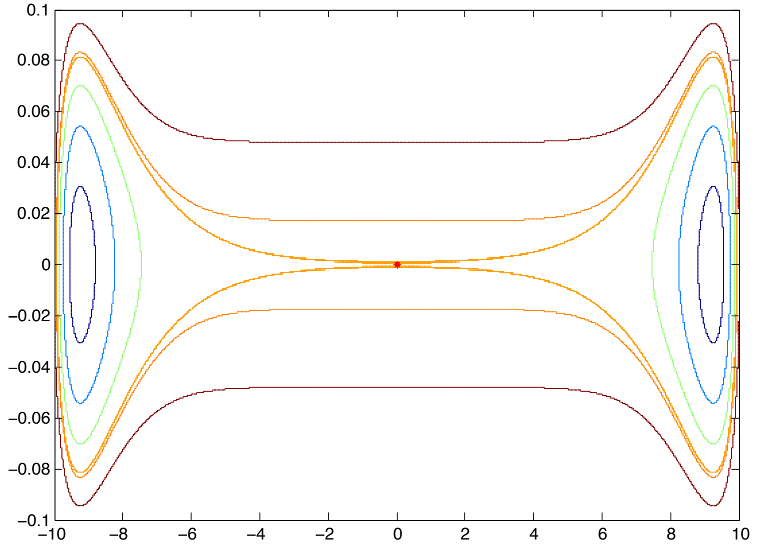
Phase Space of Average Reduced Equations (I)

- Average reduced Hamiltonian is

$$\bar{H}_2 = \frac{1}{2}y^2 + \omega I + \epsilon\left(na_0 + \sum_{k=0}^{13} c_{2k}(I)x^{2k}\right)$$

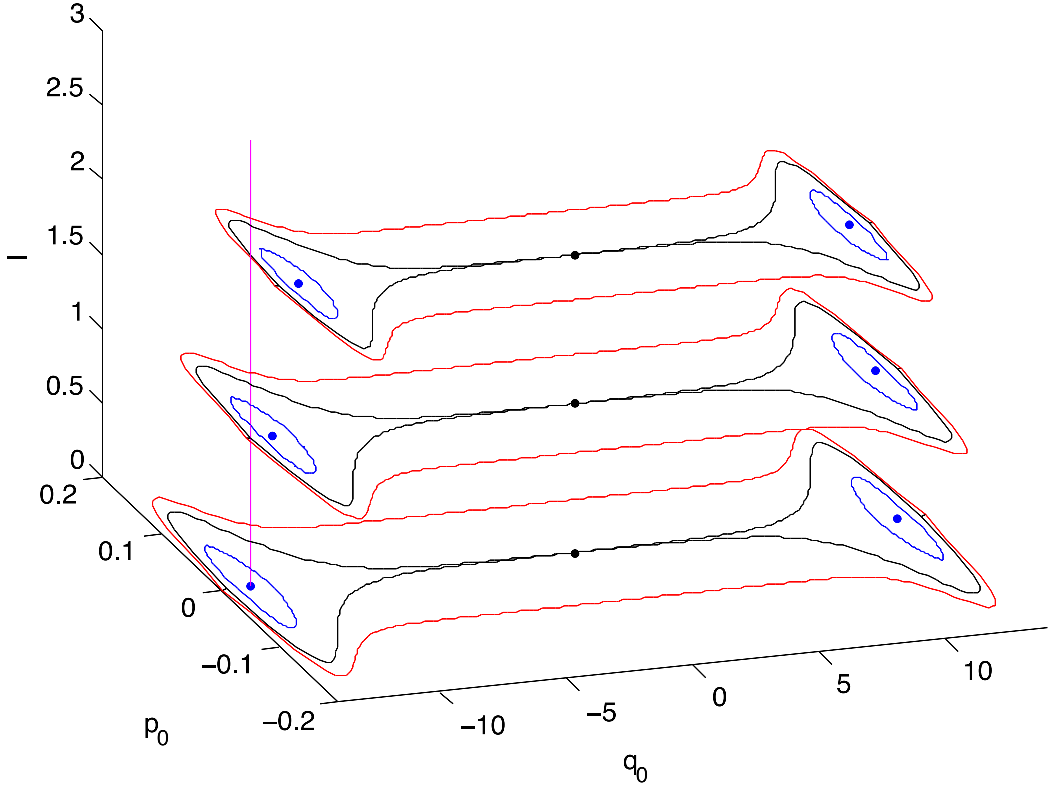
- Show the contour plots for average reduced Hamiltonian which are the phase space for average reduced equations. ($I = 0$; $I = 5$)
- **Separatrix**. 2 types of motion: **Liberation** and **Flipping**.
- Note: the separatrix "shrinks" towards the saddle as I increases.





Phase Space of Average Reduced Equations (II)

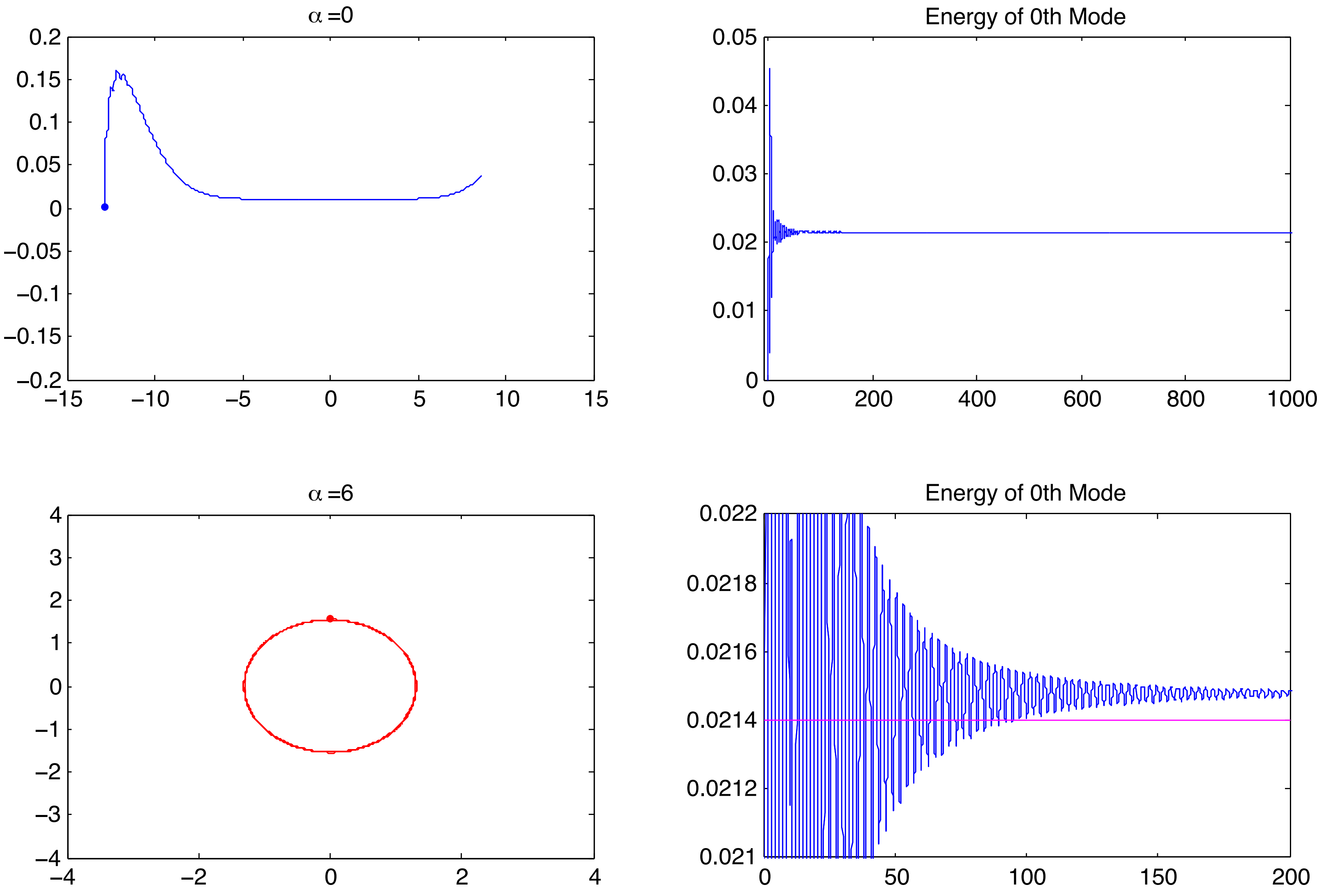
- If stacked up in increasing I (action of excited mode), we obtain



- In (x, y, I) space, vertical axis can also be seen as axis of increasing activation energy by scaling with ω, $E_{act} = \omega I$.
- The **separatrix** ”shrinks” towards the saddle as E_{act} increases. Together, (”**homoclinic** manifold”) can be used to study MAEs.

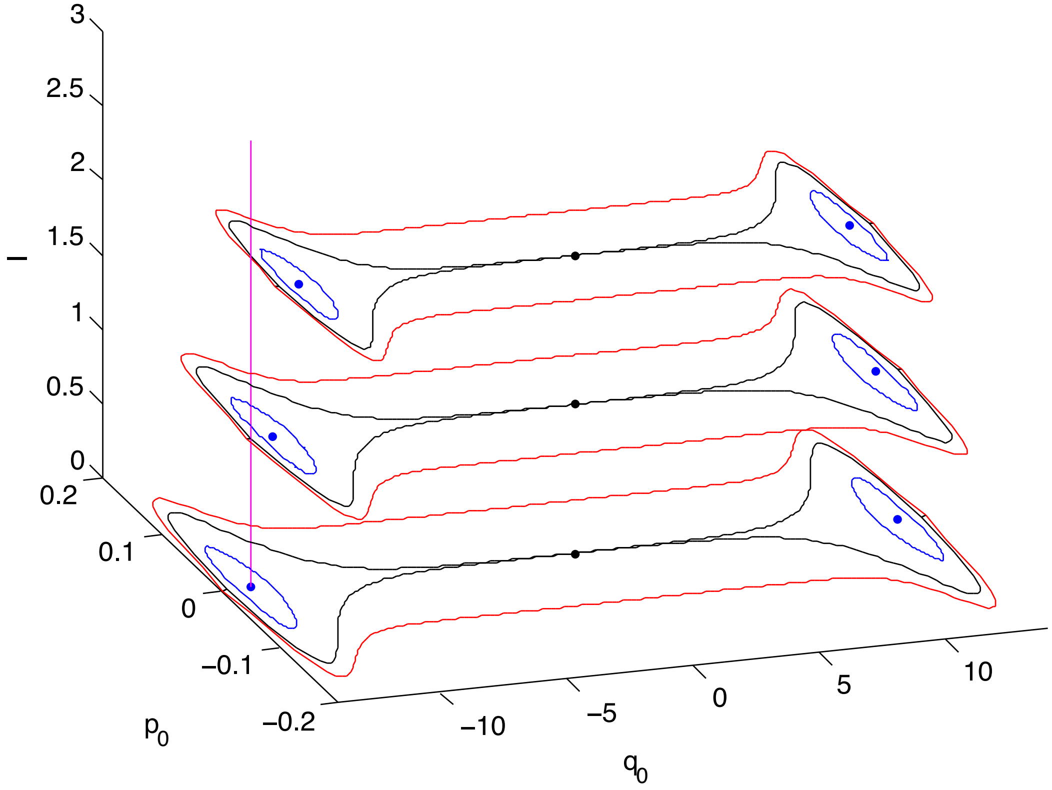
Numerical Study of MAE for 2 Mode Truncation

- For enough energy in excited mode, energy transfered to reactive mode will surpass those at saddle and the system will be driven from initial equilibrium ($\sqrt{n}\theta_e$), across separatrix, to flipping.



Analytical Study of MAE (I)

- For **average reduced system**, this process manifests itself via changes in phase spaces parametrized by I.
- For activation energy slightly larger than MAE, $(E_{min} = \omega I_m)$, initial equilibrium at $(x_e, 0)$, now parametrized by I_m^+, $(x_e, 0, I_m^+)$, will cross the **separatrix** parametrized by I_m^+,
  move into flipping region of phase space parametrized by I_m^+ and induce the DNA division.



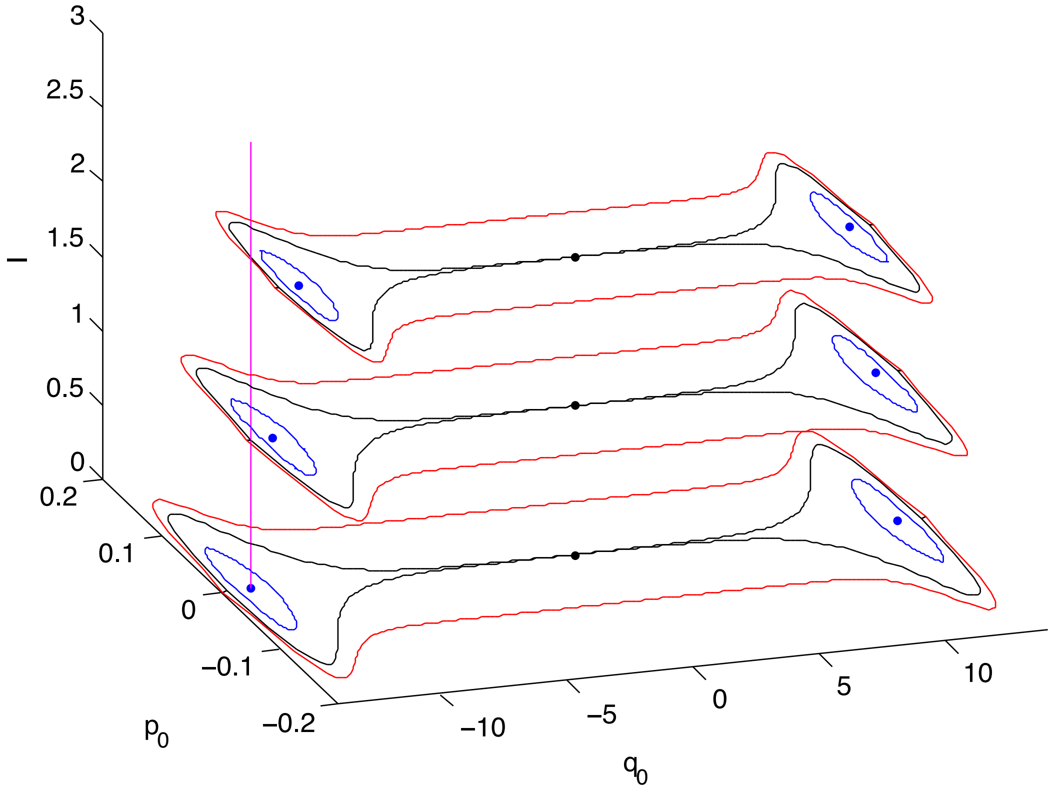
Analytical Study of MAE (II)

- MAE can be found by the **condition** that point $(x_e, 0, I_m)$ is on **separatrix** passing through saddle $(0, 0, I_m)$.
- Since **separatrix** is a curve (x, y) whose energy is those at saddle:

$$\bar{H}_2(x, y, I_m) = \bar{H}_2(0, 0, I_m),$$

- MAE can be found by solving for I_m from the **condition**

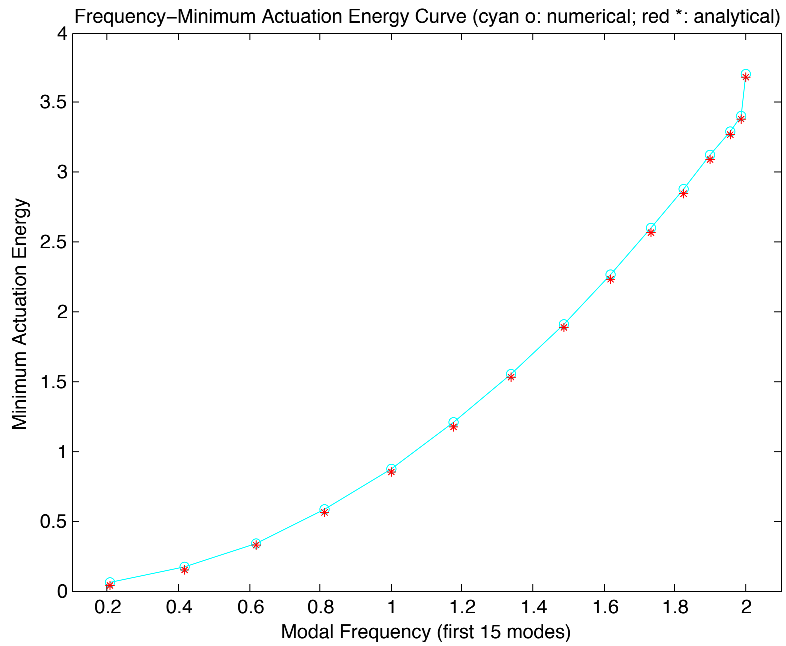
$$\bar{H}_2(x_e, 0, I_m) = \bar{H}_2(0, 0, I_m).$$

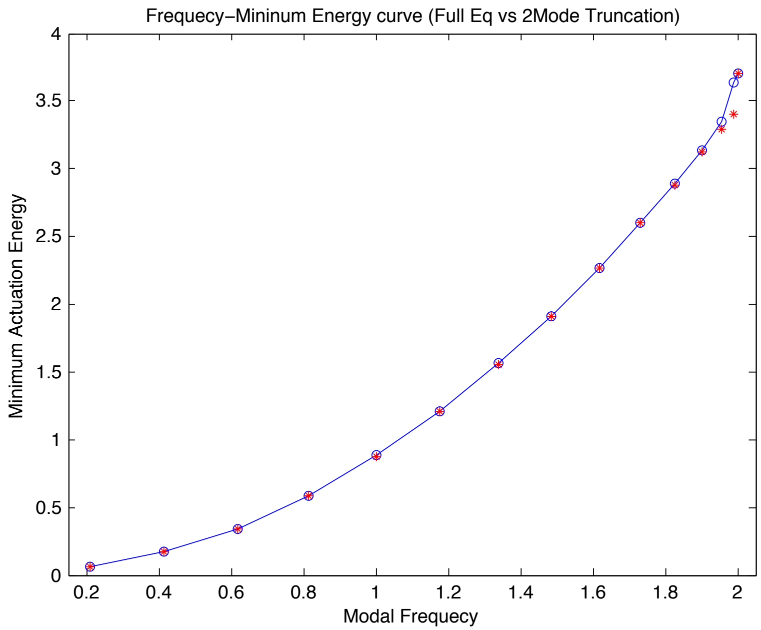


Analytical Study of MAE (III)

- Data for cyan ”o”s are from simulations (2 Mode Truncation): e.g., 6th data point (6th mode) with $\omega_6 = 1.17$ needs $E_m = 1.205$.
- Data for magenta ”*”s are from analytical computations: 6th data point with $\omega_6 = 1.17$ has $E_m = 1.1801$ (error $< 2\%$).
- Data from simulations/analytical computations match very well.
- Also, E_m (except 15th mode) can be approximated as a parabola

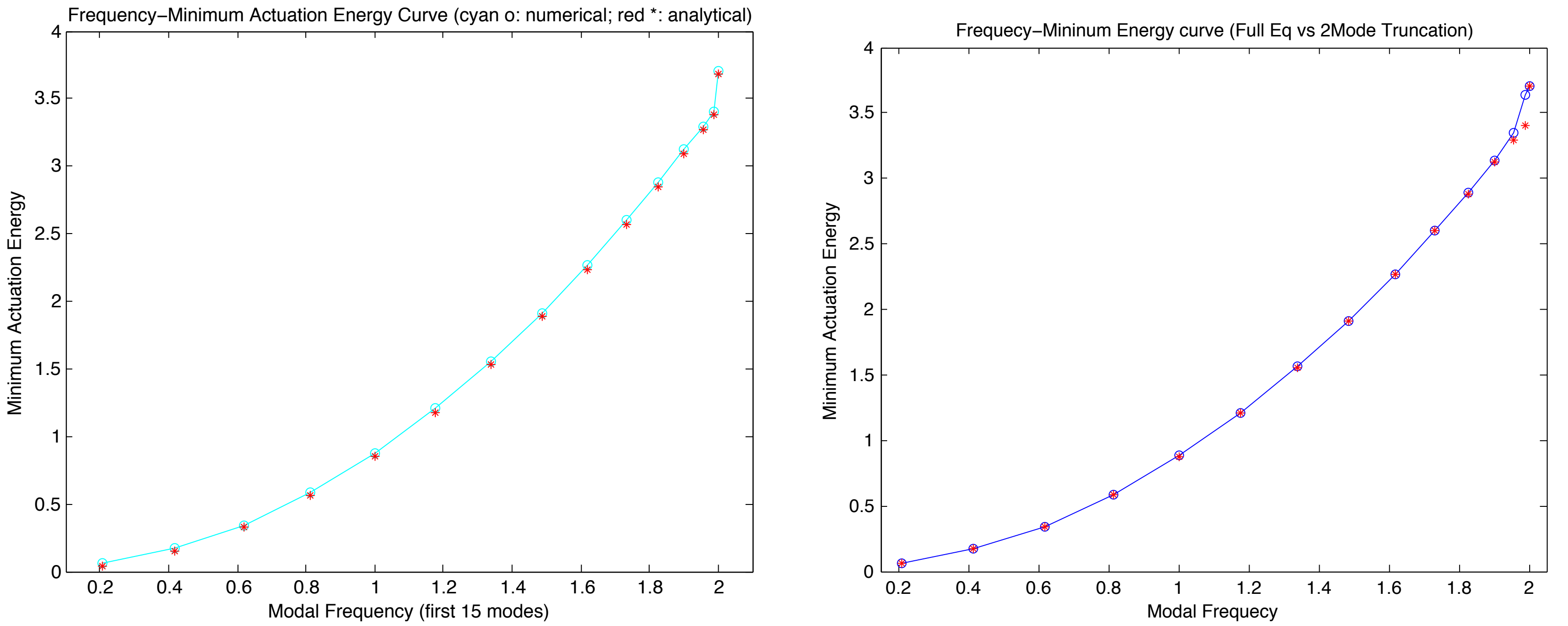
$$E_m = 0.8539 \times \omega^2$$





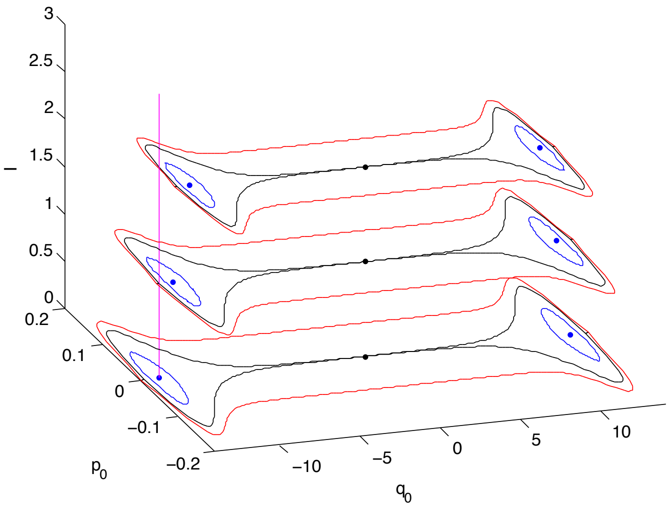
Analytical Study of MAE (IV)

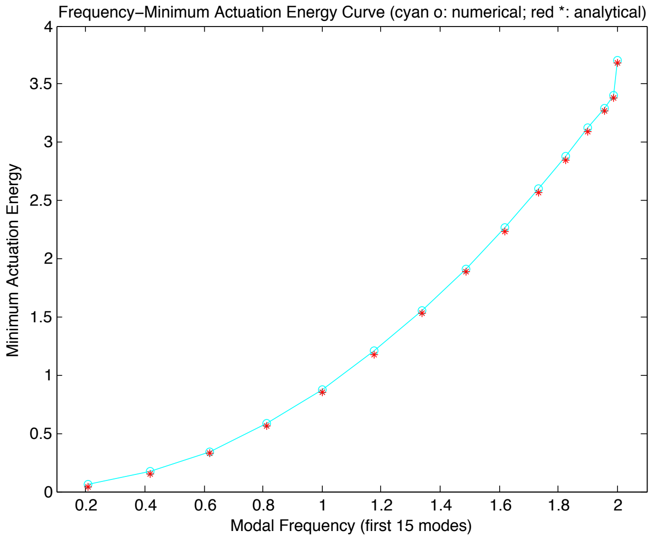
- Blue "o"s are data from simulations of full equations (30 modes): e.g., 6th data point (6th mode) with $\omega_6 = 1.17$ needs $E_m = 1.205$.
- Red "*" are from simulations of 2Mode truncations. Besides 14th mode, all other data values of blue "o"s and red "*"s have differences less than 1%.
- **Therefore**, for the study of MAEs, analytical computation provides **accurate prediction** not only for the reduced models, but also for the full system.



Summary: Analytical Results on Internal Dynamics

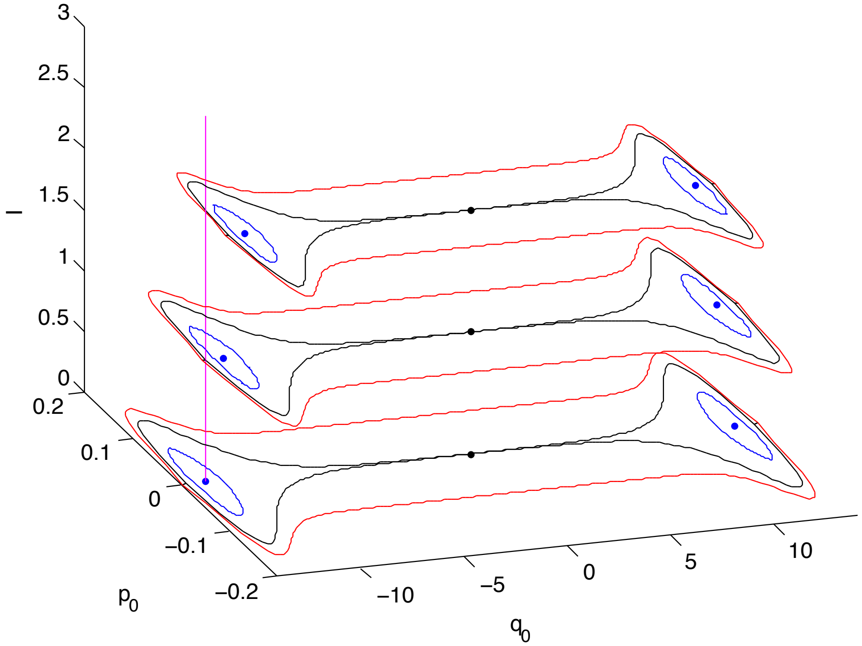
- By applying **partial averaging**, we have obtained average reduced equations for a chain of coupled Morse oscillators.
  - Reveal coupling of energy in excited mode/dynamics of reactive mode, as well as phase space structures of activation mechanism.
  - Enable us to estimate analytically MAEs, and discover a relation between modal frequencies of excited mode and MAEs.
  - These estimates match very well with the numerical simulations obtained from **reduced** and **full model**.
- The results show nearly 0 : 1 internal resonance is responsible for the phenomenon of structured activation of our DNA model.

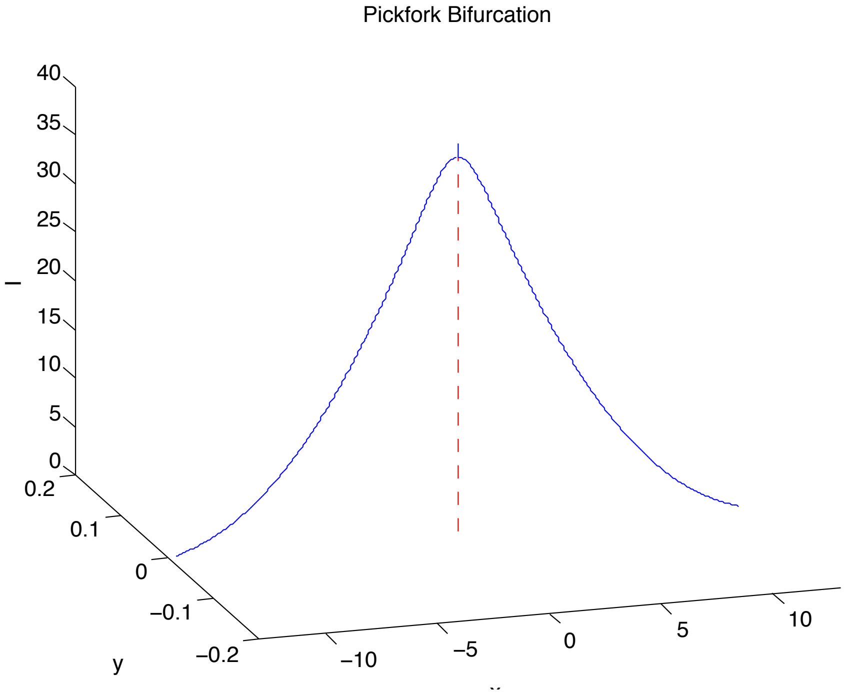




Want to Control via Parametric Resonance (PR)

- Building on understanding of internal dynamics, want to control division of this model via parametric excitation, in resonance with internal trigger modes.
- This effort is guided by 2 observations and 1 conjecture:
  - Average reduced model has a pitchfork bifurcation at $I_b = 38$: curve of stable equilibria; dashed line of saddles; bifurcates at I_b where $(0, 0, I_b^+)$ becomes stable.
  - PR is an efficient way for energy transfer from external source.




Pickfork Bifurcation

Want to Control via Parametric Resonance (PR)

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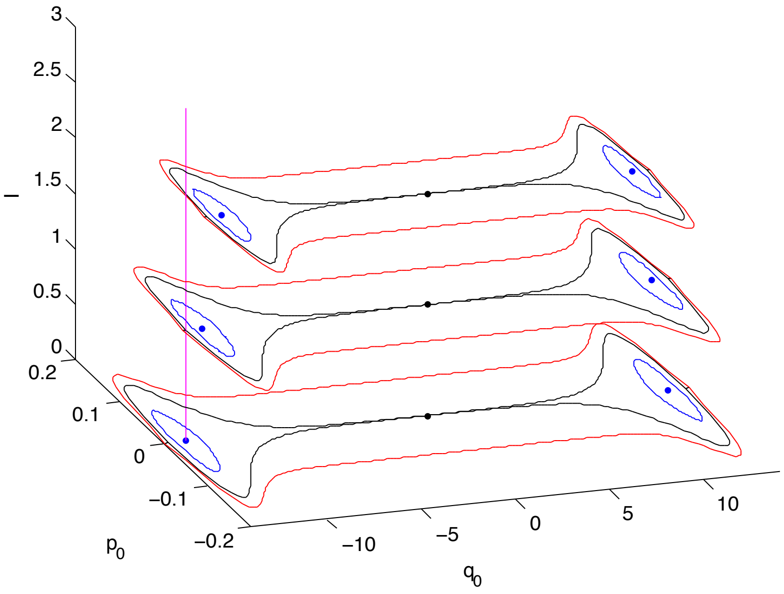
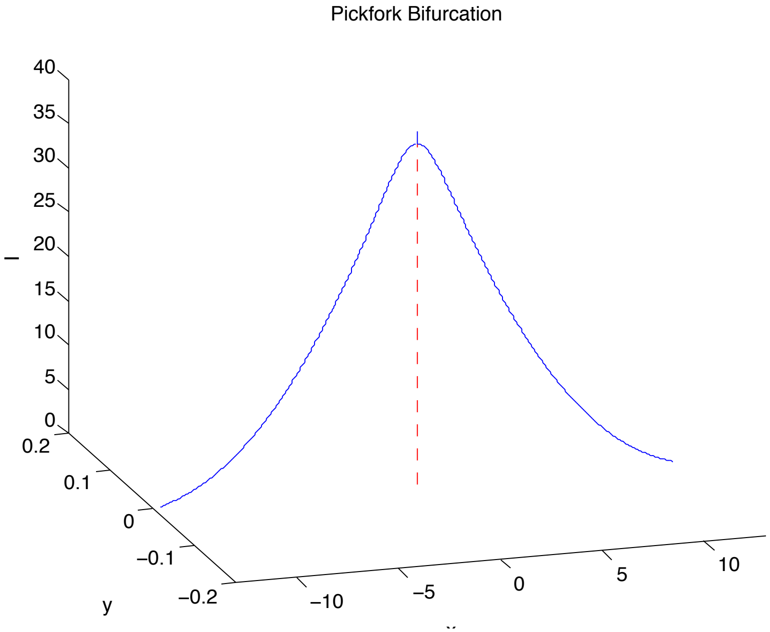
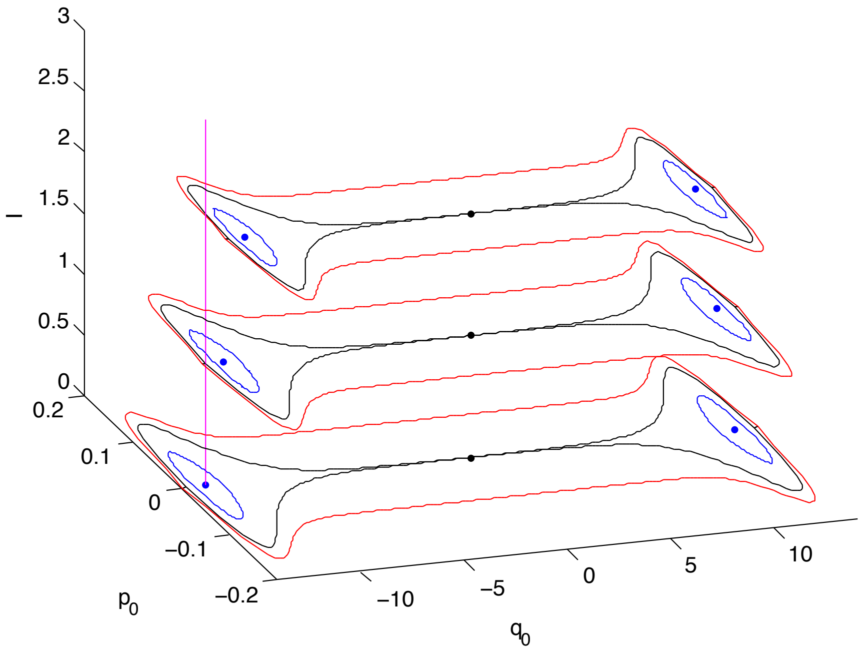
- This effort is guided by 2 observations and 1 conjecture:
  - Average reduced model has a pitchfork bifurcation at $I = 38$.
  - PR is an efficient way for energy transfer from external source.
- Conjecture: EM/Enzyme use PR to pump energy into trigger mode and stabilize the chain at open state (for replication/transcription).

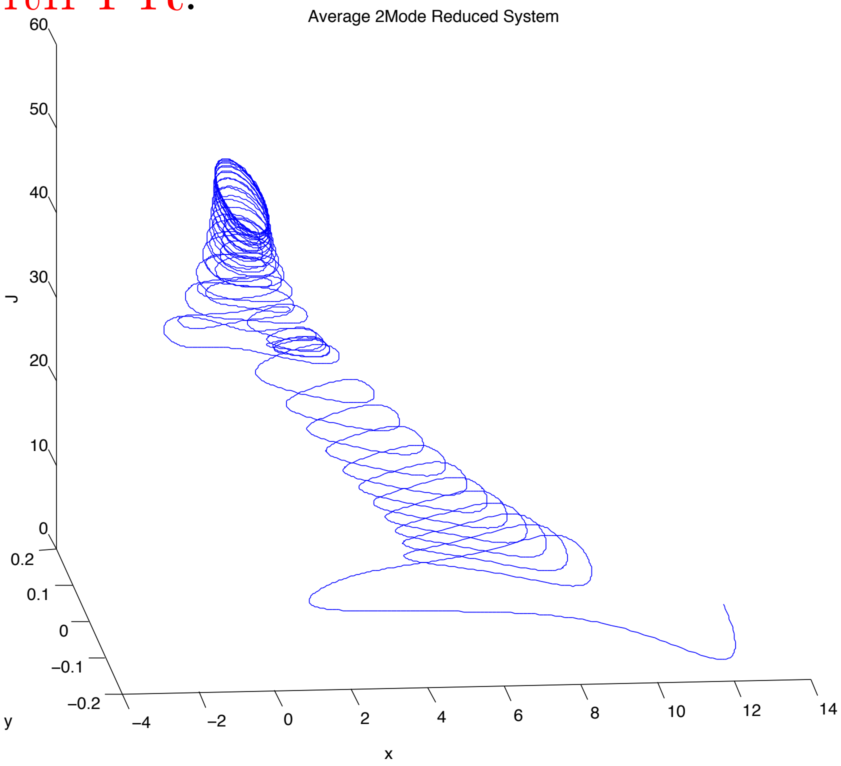




3 Main Results on Control via PR

- By choosing appropriate excitations, able to generate a class of trajectories that show how PR drive Average Reduced Model from its (almost) equilibrium state to its open state $(0, 0)$.
- By using a new PR Hamiltonian for our Average Reduced Model, we study global phase space structures of our model and shed lights on the interesting trajectories mentioned above.
- Able to extend results for Average Reduced Model with PR to the Reduced as well as Full Model with PR.





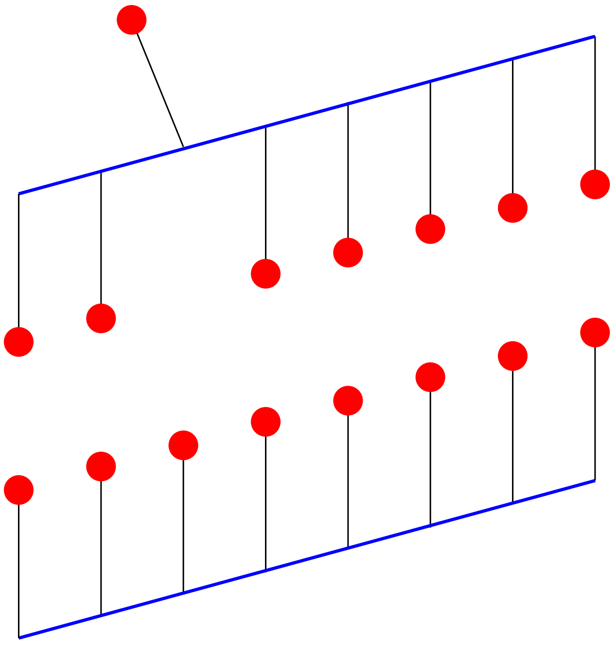
EOM of Full Model with Parametric Excitation (PE)

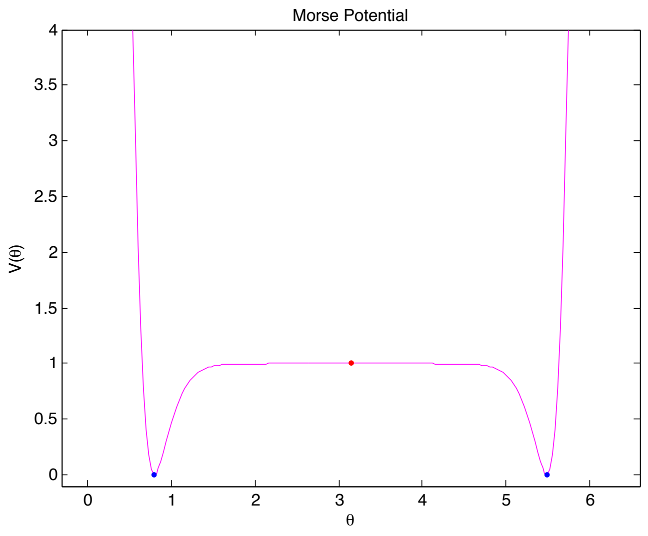
- EOM of full model with PE and frictions can be written as

$$\ddot{\theta}_i + D_{ij}\theta_j - \epsilon U(\theta_i) = \epsilon\delta\theta_i f \cos\Omega t - \epsilon\delta\mu\dot{\theta}_i$$

where $i = 1, ..., n$;

- LHS is original EOM (without PE or frictions);
- f, Ω are amplitude/frequency;
  Ω in 1:2 resonance with frequency ω of a chosen internal mode.
- μ is frictional coefficient; δ is another small parameter.





EOM of Average Reduced Model with PE

- After using FMC, EOM of 2Mode Reduced Model is given by

$$\dot{x} = y \qquad \dot{y} = -\epsilon M_x - \epsilon\delta\mu y + \epsilon\delta f x \cos\Omega t.$$
$$\dot{q} = p \qquad \dot{p} = -\omega^2 q - \epsilon M_q - \epsilon\delta\mu p + \epsilon\delta f q \cos\Omega t.$$

- Applying partial averaging, we obtain **Average Reduced EOM**

$$\dot{x} = y, \qquad \dot{\beta} = \epsilon(\bar{M}_I - \sigma/2\omega + \delta f \cos 2\beta/4\omega),$$
$$\dot{y} = -\epsilon(\bar{M}_x + \delta\mu y), \qquad \dot{I} = \epsilon I(\delta f \sin 2\beta/2\omega - \delta\mu).$$

where I, β, action/phase of trigger mode;
σ is a detuning parameter, defined by $\Omega^2/4 = \omega^2 + \epsilon\sigma$.

- Average Reduced System (without friction) has a PR Hamiltonian

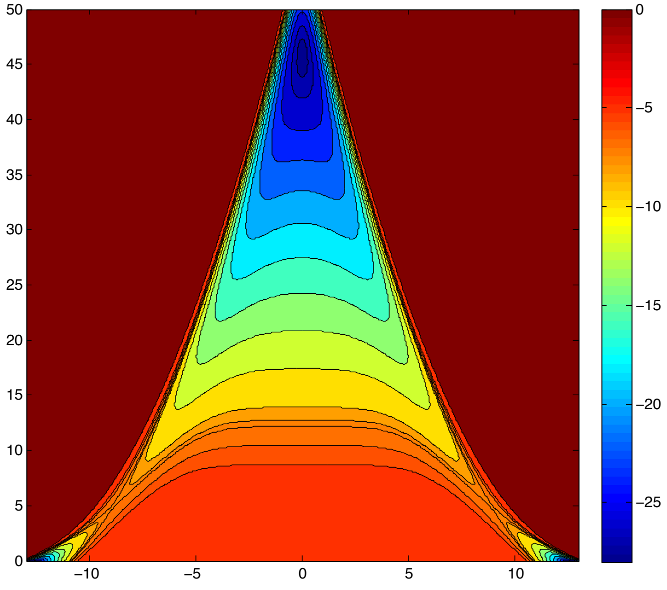
$$H = \frac{1}{2}y^2 + \epsilon\bar{M} - \epsilon\frac{\sigma}{2\omega}I + \epsilon\delta f\frac{I\cos 2\beta}{4\omega}$$

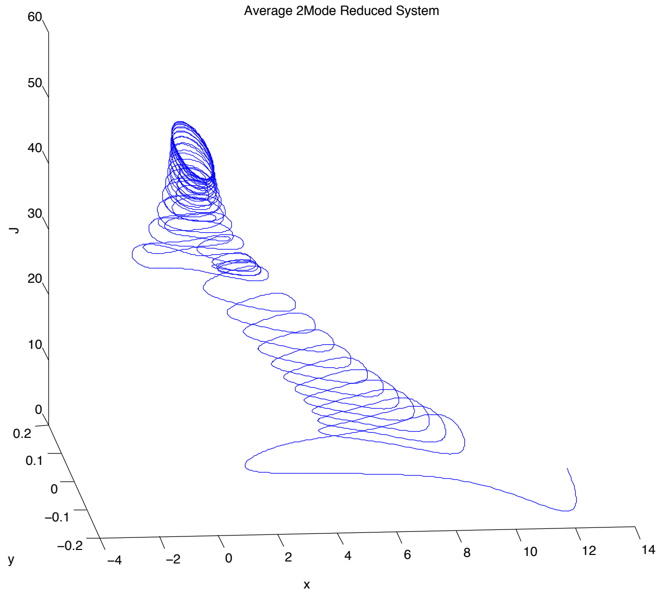
that can provide insights on global phase space structures of this average reduced model.

Parametric Resonance Drive DNA to Division

- Detailed local bifurcation analysis reveals ranges of σ and other parameters, f, μ, δ, where **desired dynamics** may be available.
- **Energy contour** of effective potential of PR Hamiltonian provides insights for global phase space structures.
  - PE turns $(x, J) = (0, J_e)$ which marks DNA division into a sink;
  - it creates a low barrier rank 1 saddle closes to the DNA stable equilibrium state $(12.6, 0)$.

This bifurcation allows trajectory with a little energy to move from an almost equilibrium state over the saddle and reach the sink.



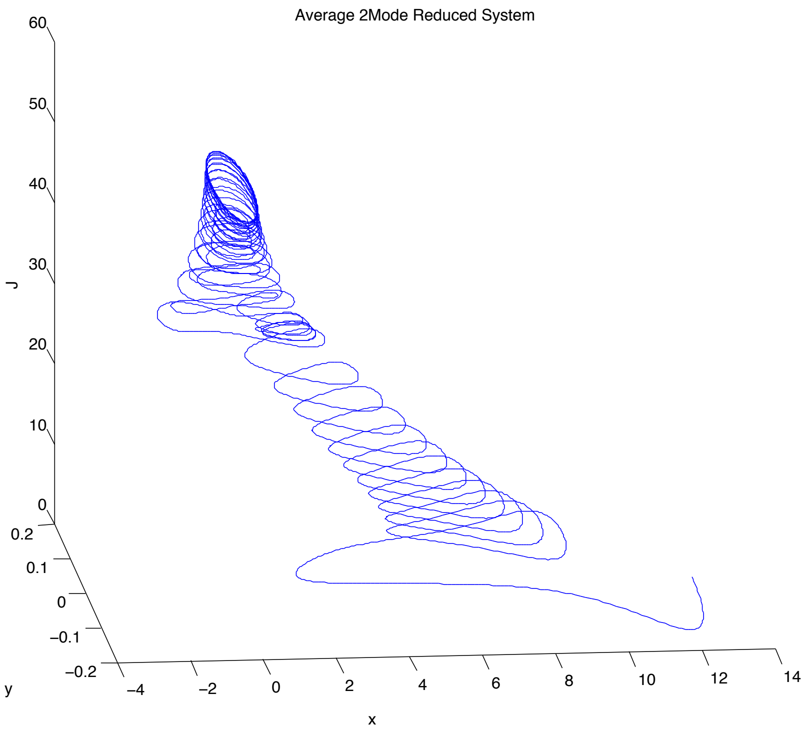


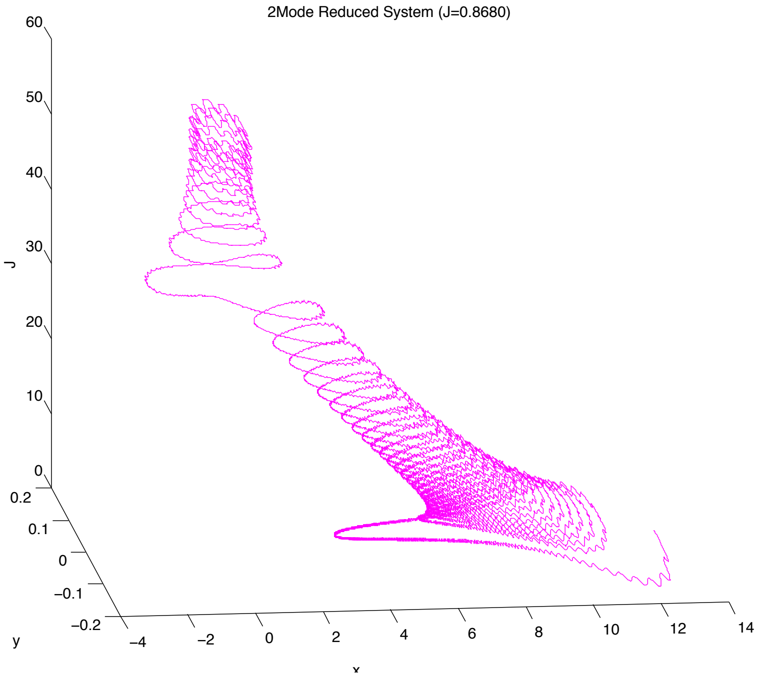
Extend Results to Reduced Model

- Recall: EOM for Reduced Model are

$$\begin{aligned} \dot{x} &= y & \dot{y} &= -\epsilon M_x - \epsilon\delta\mu y + \epsilon\delta f x \cos\Omega t \\ \dot{q} &= p & \dot{p} &= -\omega^2 q - \epsilon M_q - \epsilon\delta\mu p + \epsilon\delta f q \cos\Omega t. \end{aligned}$$

- Left: a trajectory for average reduced model.
- Right: a corresponding trajectory for reduced model.



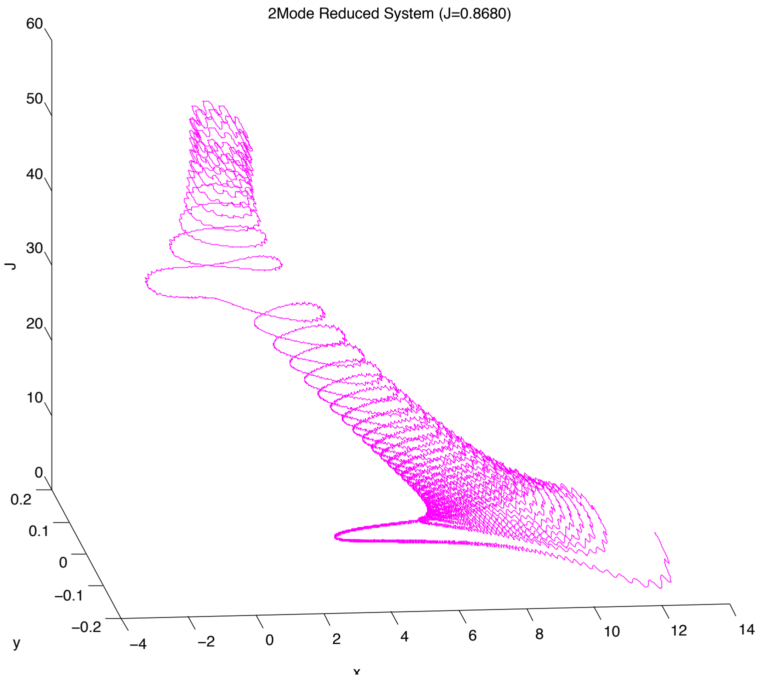


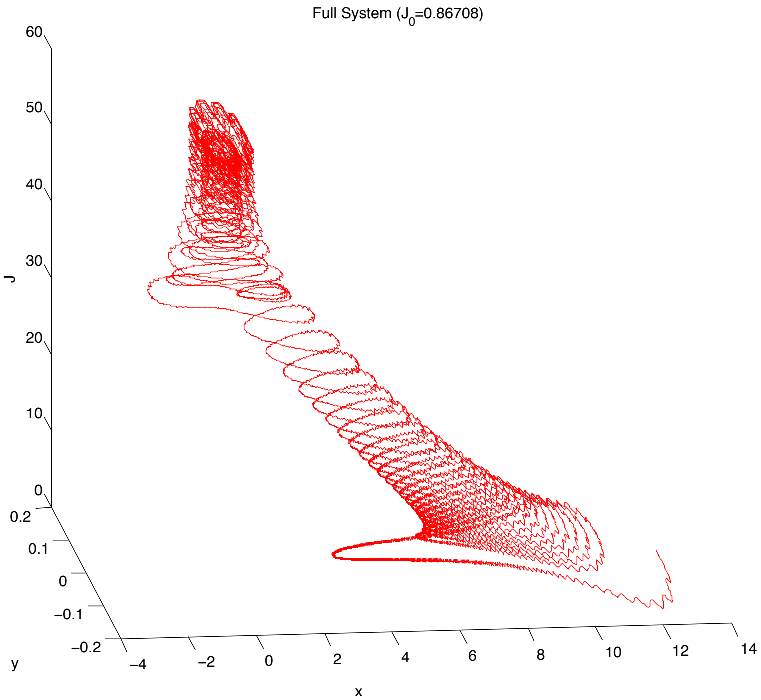
Extend Results to Full Model

- Recall: EOM of full model in original coordinates are given by

$$\ddot{\theta}_i + D_{ij}\theta_j = \epsilon U(\theta_i) + \epsilon\delta\theta_i f \cos\Omega t - \epsilon\delta\mu\dot{\theta}_i$$

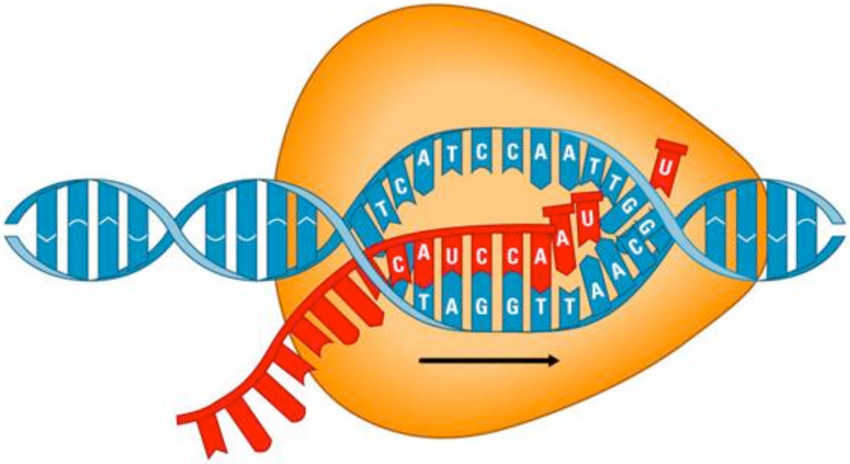
- A trajectory for reduced model and a corr. one for full model.
- More studies needed for tradeoffs between amplitude f, detuning parameter σ, frictional coeff. μ on one hand and initial action-phase I_0, β_0 (and mixed modes) on the other.

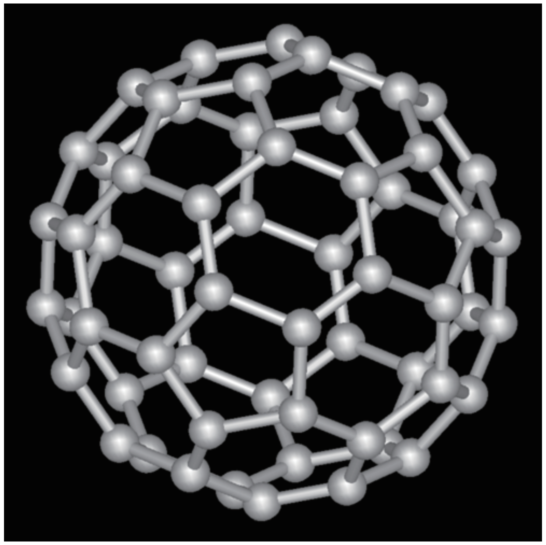




Summary and Future Work

- Study internal resonance, energy transfer, activation mechanism, and control of a model of DNA division via PR.
- Future work: add effects of **inhomogeneity** and **helicity**.
  - Moment, torsional/base pair interactions depend on positions.
- Methodology forged in this study (which merges geometric reduction, partial averaging, chaotic transport, and control via PR) should be applicable to many molecular and biomolecular systems, as well as other mechanical systems involving **multiple-scale**.





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